### **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT) (51) International Patent Classification 6: WO 98/18323 (11) International Publication Number: A01N 43/04, A61K 31/70, C12Q 1/68 A1 7 May 1998 (07.05.98) (43) International Publication Date: (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, PCT/US97/19575 (21) International Application Number: BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, (22) International Filing Date: 28 October 1997 (28.10.97) LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, (30) Priority Data: 28 October 1996 (28.10.96) US 08/739,150

US

US

(71) Applicant (for all designated States except US): ASTRA AKTIEBOLAG [SE/SE]; S-151 85 Södertälje (SE).

6 December 1996 (06.12.96)

14 July 1997 (14.07.97)

(72) Inventors; and

08/759,739

08/891,928

- (75) Inventors/Applicants (for US only): SMITH, Douglas [US/US]; 2 Mayflower Lane, Gloucester, MA 01930 (US). ALM, Richard, A. [AU/US]; 28 Russet Hill Road, Ashland, MA 01721 (US).
- (74) Agents: MANDRAGOURAS, Amy, E. et al.; Lahive & Cockfiel, LLP, 28 State Street, Boston, MA 02109 (US).

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

#### **Published**

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

- (54) Title: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPOSITIONS THEREOF
- (57) Abstract

Recombinant or substantially pure preparations of *H. pylori* polypeptides are described. The nucleic acids encoding the polypeptides also are described. The *H. pylori* polypeptides are useful for diagnostics and vaccine compositions.

## FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

$\mathbf{AL}$	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal .
AU	Australia	GA	Gabon	LV	Latvia	SZ.	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
ВÉ	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland .	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT.	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	Ϋ́U	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		•
CM	Cameroon	*	Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	u	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		•
EE	Estonia	LR.	Liberia	SG	Singapore		

10

15

20

25

30

35

### NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPOSITIONS THEREOF

### Background of the Invention

Helicobacter pylori is a gram-negative, S-shaped, microaerophilic bacterium that was discovered and cultured from a human gastric biopsy specimen. (Warren, J.R. and B. Marshall, (1983) Lancet 1: 1273-1275; and Marshall et al., (1984) Microbios Lett. 25: 83-88). H. pylori has been strongly linked to chronic gastritis and duodenal ulcer disease. (Rathbone et. al., (1986) Gut 27: 635-641). Moreover, evidence is accumulating for an etiologic role of H. pylori in nonulcer dyspepsia, gastric ulcer disease, and gastric adenocarcinoma. (Blaser M. J., (1993) Trends Microbiol. 1: 255-260). Transmission of the bacteria occurs via the oral route, and the risk of infection increases with age. (Taylor, D.N. and M. J. Blaser, (1991) Epidemiol. Rev 13: 42-50). H. pylori colonizes the human gastric mucosa, establishing an infection that usually persists for decades. Infection by H. pylori is prevalent worldwide. Developed countries have infection rates over 50% of the adult population, while developing countries have infection rates reaching 90% of the adults over the age of 20. (Hopkins R. J. and J. G. Morris (1994) Am. J. Med. 97: 265-277).

The bacterial factors necessary for colonization of the gastric environment, and for virulence of this pathogen, are poorly understood. Examples of the putative virulence factors include the following: urease, an enzyme that may play a role in neutralizing gastric acid pH (Eaton et al., (1991) *Infect. Immunol.* 59: 2470-2475; Ferrero, R.L. and A. Lee (1991) *Microb. Ecol. Hlth. Dis.* 4: 121-134; Labigne et al., (1991) *J. Bacteriol.* 173: 1920-1931); the bacterial flagellar proteins responsible for motility across the mucous layer. (Hazell et al., (1986) *J. Inf. Dis.* 153: 658-663; Leying et al., (1992) *Mol. Microbiol.* 6: 2863-2874; and Haas et al., (1993) *Mol. Microbiol.* 8: 753-760); Vac A, a bacterial toxin that induces the formation of intracellular vacuoles in epithelial cells (Schmitt, W. and R. Haas, (1994) *Molecular Microbiol.* 12(2): 307-319); and several gastric tissue-specific adhesins. (Boren et al., (1993) *Science* 262: 1892-1895; Evans et al., (1993) *J. Bacteriol.* 175: 674-683; and Falk et al., (1993) *Proc. Natl. Acad. Sci.* USA 90: 2035-203).

Numerous therapeutic agents are currently available that eradicate *H. pylori* infections *in vitro*. (Huesca et. al., (1993) *Zbl. Bakt.* 280: 244-252; Hopkins, R. J. and J. G. Morris, supra). However, many of these treatments are suboptimally effective *in vivo* because of bacterial resistance, altered drug distribution, patient non-compliance or poor drug availabilty. (Hopkins, R. J. and J. G. Morris, supra). Treatment with antibiotics combined with bismuth are part of the standard regime used to treat *H. pylori* infection.

(Malfertheiner, P. and J. E. Dominguez-Munoz (1993) Clinical Therapeutics 15 Supp. B: 37-48). Recently, combinations of a proton pump inhibitors and a single antibiotic have been shown to ameliorate duodenal ulcer disease. (Malfertheiner, P. and J. E. Dominguez-Munoz supra). However, methods employing antibiotic agents can have the problem of the emergence of bacterial strains which are resistant to these agents. (Hopkins, R. J. and J. G. Morris, supra). These limitations demonstrate that new more effective methods are needed to combat *H. pylori* infections *in vivo*. In particular, the design of new vaccines that may prevent infection by this bacterium is highly desirable.

### 10 Summary of the Invention

15

20

25

30

This invention relates to novel genes, e.g., genes encoding polypeptides such as bacterial surface proteins, from the organism *Helicobacter pylori* (*H. pylori*), and other related genes, their products, and uses thereof. The nucleic acids and peptides of the present invention have utility for diagnostic and therapeutics for *H. pylori* and other *Helicobacter* species. They can also be used to detect the presence of *H. pylori* and other *Helicobacter* species in a sample; and for use in screening compounds for the ability to interfere with the *H. pylori* life cycle or to inhibit *H. pylori* infection. More specifically, this invention features compositions of nucleic acids corresponding to entire coding sequences of *H. pylori* proteins, including surface or secreted proteins or parts thereof, nucleic acids capable of binding mRNA from *H. pylori* proteins to block protein translation, and methods for producing *H. pylori* proteins or parts thereof using peptide synthesis and recombinant DNA techniques. This invention also features antibodies and nucleic acids useful as probes to detect *H. pylori* infection. In addition, vaccine compositions and methods for the protection or treatment of infection by *H. pylori* are within the scope of this invention.

### Detailed Description of the Drawings

Figure 1 is a bar graph that depicts the antibody titer in serum of mice following immunization with specific *H. pylori* antigens.

Figure 2 is a bar graph that depicts the antibody titer in mucous of mice following immunization with specific *H. pylori* antigens.

Figure 3 is a bar graph that depicts therapeutic immunization of *H. pylori* infected mice with specific antigens dissolved in HEPES buffer.

Figure 4 is a bar graph that depicts therapeutic immunization of *H. pylori* infected mice with specific antigens dissolved in buffer containing DOC.

5.

10

15

20

25

30

35

Figure 5 depicts the amino acid sequence alignment in a portion of the sequence of five *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

Figure 6 depicts the amino acid sequence alignment in a portion of the sequence of four *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

Figure 7 depicts the amino acid sequence alignment in a portion of the sequence of two *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

Figure 8 depicts the amino acid sequence alignment in a portion of the sequence of two *H. pylori* proteins (depicted in the single letter amino acid code; shown N-terminal to C-terminal, left to right).

#### **Detailed Description of the Invention**

In one aspect, the invention features a recombinant or substantially pure preparation of *H. pylori* polypeptide of SEQ ID NO: 74. The invention also includes substantially pure nucleic acid encoding an *H. pylori* polypeptide of SEQ ID NO: 74, such nucleic acid is contained in SEQ ID NO: 1. The *H. pylori* polypeptide sequences of the invention described herein are contained in the Sequence Listing, and the nucleic acids encoding *H. pylori* polypeptides of the invention are contained in the Sequence Listing.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 75, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 2.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 76, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 3.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 77, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 4.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 78, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 5.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 79, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 6.

10

15

20:

25

30

35

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 80, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 7.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 81, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 8.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 82, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 9.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 83, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 10.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 84, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 11.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 85, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 12.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 86, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 13.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 87, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 14.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 88, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 15.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 89, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 16.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 90, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 17.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 91, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 18.

10

15

20

25

30

35

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 92, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 19.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 93, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 20.

In another aspect, the invention features a substantially pure nucleic acid éncoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 94, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 21.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 95, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 22.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 96, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 23.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 97, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 24.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 98, such as a nucleic acid comprising a nucleotide sequence of SEO ID NO: 25.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 99, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 26.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 100, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 27.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 101, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 28.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 102, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 29.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 103, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 30.

15

20

25

30

35

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 104, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 31.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 105, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 32.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 106, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 33.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 107, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 34.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 108, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 35.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 109, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 36.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 110, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 37.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 111, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 38.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 112, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 39.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 113, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 40.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 114, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 41.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 115, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 42.

10

15

20

25

30

35

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 116, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO:43.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 117, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 44.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 118, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 45.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 119, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 46.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 120, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 47.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 121, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 48.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 122, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 49.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 123, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 50.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 124, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 51.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 125, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 52.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 126, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 53.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 127, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 54.

10

15

20

25

30

35

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 128, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 55.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 129, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 56.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 130, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 57.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 131, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 58.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 132, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 59.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 133, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 134, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 61.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 135, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 62.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 136, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 63.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 137, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 64.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 138, such as a nucleic acid comprising a nucleotide sequence of SEO ID NO: 65.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 139, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 66.

15

20

25

30

35

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 140, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 67.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 141, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 68.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 142, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 69.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 143, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 70.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 144, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 71.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 145, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 72.

In another aspect, the invention features a substantially pure nucleic acid encoding an *H. pylori* polypeptide having an amino acid sequence of SEQ ID NO: 146, such as a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 73.

Particularly perferred is an isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof. Such nucleic acid is selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10,

10

15

30

35

SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71.

In another embodiment, the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO:71.

In yet another embodiment, the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by the nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, and SEQ ID NO: 58.

Particularly preferred is an isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof. Such nucleic acid is selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40. SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68.

Particularly preferred is an isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof. Such nucleic acid is selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73.

Particularly preferred is a purified or isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein the polypeptide is selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID

10

15

20

25

30

35

NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.

In another embodiment, the *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.

In another embodiment, the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, and SEQ ID NO:144.

In another embodiment, the *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131.

Particularly preferred is a purified or isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein the polypeptide is selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.

Particularly preferred is a purified or isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein the polypeptide is selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ

15

20

25

30

35

ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.

In another aspect, the invention pertains to any individual *H. pylori* polypeptide member or nucleic acid encoding such a member from the above-identified groups of *H. pylori* polypeptides.

In another aspect, the invention features nucleic acids capable of binding mRNA of *H. pylori*. Such nucleic acid is capable of acting as antisense nucleic acid to control the translation of mRNA of *H. pylori*. A further aspect features a nucleic acid which is capable of binding specifically to an *H. pylori* nucleic acid. These nucleic acids are also referred to herein as complements and have utility as probes and as capture reagents.

In another aspect, the invention features an expression system comprising an open reading frame corresponding to *H. pylori* nucleic acid. The nucleic acid further comprises a control sequence compatible with an intended host. The expression system is useful for making polypeptides corresponding to *H. pylori* nucleic acid.

In another aspect, the invention features a cell transformed with the expression system to produce *H. pylori* polypeptides.

In another aspect, the invention features a method of generating antibodies against *H. pylori* polypeptides which are capable of binding specifically to *H. pylori* polypeptides. Such antibodies have utility as reagents for immunoassays to evaluate the abundance and distribution of *H. pylori*-specific antigens.

In another aspect, the invention features a method of generating vaccines for immunizing an individual against *H. pylori*. The vaccination method includes: immunizing a subject with at least one *H. pylori* polypeptide according to the present invention, e.g., a surface or secreted polypeptide, or active portion thereof, and a pharmaceutically acceptable carrier. Such vaccines have therapeutic and/or prophylactic utilities.

In another aspect, the invention provides a method for generating a vaccine comprising a modified immunogenic *H. pylori* polypeptide, e.g., a surface or secreted polypeptide, or active portion thereof, and a pharmacologically acceptable carrier.

In another aspect, the invention features a method of evaluating a compound, e.g. a polypeptide, e.g., a fragment of a host cell polypeptide, for the ability to bind an *H. pylori* polypeptide. The method includes: contacting the candidate compound with an *H. pylori* polypeptide and determining if the compound binds or otherwise interacts with an *H. pylori* polypeptide. Compounds which bind *H. pylori* are candidates as activators or inhibitors of the bacterial life cycle. These assays can be performed *in vitro* or *in vivo*.

10

15

20

25

30

35

In another aspect, the invention features a method of evaluating a compound, e.g. a polypeptide, e.g., a fragment of a host cell polypeptide, for the ability to bind an *H. pylori* nucleic acid, e.g., DNA or RNA. The method includes: contacting the candidate compound with an *H. pylori* nucleic acid and determining if the compound binds or otherwise interacts with an *H. pylori* polypeptide. Compounds which bind *H. pylori* are candidates as activators or inhibitors of the bacterial life cycle. These assays can be performed *in vitro* or *in vivo*.

The invention features H. pylori polypeptides, preferably a substantially pure preparation of an H. pylori polypeptide, or a recombinant H. pylori polypeptide. In preferred embodiments: the polypeptide has biological activity; the polypeptide has an amino acid sequence at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% identical or homologous to an amino acid sequence of the invention contained in the Sequence Listing, preferably it has about 65% sequence identity with an amino acid sequence of the invention contained in the Sequence Listing, and most preferably it has about 92% to about 99% sequence identity with an amino acid sequence of the invention contained in the Sequence Listing; the polypeptide has an amino acid sequence essentially the same as an amino acid sequence of the invention contained in the Sequence Listing; the polypeptide is at least 5, 10, 20, 50, 100, or 150 amino acid residues in length; the polypeptide includes at least 5, preferably at least 10, more preferably at least 20, more preferably at least 50, 100, or 150 contiguous amino acid residues of the invention contained in the Sequence Listing. In yet another preferred embodiment, the amino acid sequence which differs in sequence identity by about 7% to about 8% from the H. pylori amino acid sequences of the invention contained in the Sequence Listing is also encompassed by the invention.

In preferred embodiments: the *H. pylori* polypeptide is encoded by a nucleic acid of the invention contained in the Sequence Listing, or by a nucleic acid having at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% homology with a nucleic acid of the invention contained in the Sequence Listing.

In a preferred embodiment, the subject *H. pylori* polypeptide differs in amino acid sequence at 1, 2, 3, 5, 10 or more residues from a sequence of the invention contained in the Sequence Listing. The differences, however, are such that the *H. pylori* polypeptide exhibits an *H. pylori* biological activity, e.g., the *H. pylori* polypeptide retains a biological activity of a naturally occurring *H. pylori* polypeptide.

In preferred embodiments, the polypeptide includes all or a fragment of an amino acid sequence of the invention contained in the Sequence Listing; fused, in reading frame, to additional amino acid residues, preferably to residues encoded by genomic

15

20

25

30

35

DNA 5' or 3' to the genomic DNA which encodes a sequence of the invention contained in the Sequence Listing.

In yet other preferred embodiments, the *H. pylori* polypeptide is a recombinant fusion protein having a first *H. pylori* polypeptide portion and a second polypeptide portion, e.g., a second polypeptide portion having an amino acid sequence unrelated to *H. pylori*. The second polypeptide portion can be, e.g., any of glutathione-S-transferase, a DNA binding domain, or a polymerase activating domain. In preferred embodiment the fusion protein can be used in a two-hybrid assay.

Polypeptides of the invention include those which arise as a result of alternative transcription events, alternative RNA splicing events, and alternative translational and postranslational events.

The invention also encompasses an immunogenic component which includes at least one *H. pylori* polypeptide in an immunogenic preparation; the immunogenic component being capable of eliciting an immune response specific for the *H. pylori* polypeptide, e.g., a humoral response, an antibody response, or a cellular response. In preferred embodiments, the immunogenic component comprises at least one antigenic determinant from a polypeptide of the invention contained in the Sequence Listing.

In another aspect, the invention provides a substantially pure nucleic acid having a nucleotide sequence which encodes an *H. pylori* polypeptide. In preferred embodiments: the encoded polypeptide has biological activity; the encoded polypeptide has an amino acid sequence at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% homologous to an amino acid sequence of the invention contained in the Sequence Listing; the encoded polypeptide has an amino acid sequence essentially the same as an amino acid sequence of the invention contained in the Sequence Listing; the encoded polypeptide is at least 5, 10, 20, 50, 100, or 150 amino acids in length; the encoded polypeptide comprises at least 5, preferably at least 10, more preferably at least 20, more preferably at least 50, 100, or 150 contiguous amino acids of the invention contained in the Sequence Listing.

In preferred embodiments: the nucleic acid of the invention is that contained in the Sequence Listing; the nucleic acid is at least 60%, 70%, 80%, 90%, 95%, 98%, or 99% homologous with a nucleic acid sequence of the invention contained in the Sequence Listing.

In a preferred embodiment, the encoded *H. pylori* polypeptide differs (e.g., by amino acid substitution, addition or deletion of at least one amino acid residue) in amino acid sequence at 1, 2, 3, 5, 10 or more residues, from a sequence of the invention contained in the Sequence Listing. The differences, however, are such that: the *H*.

WO 98/18323 PCT/US97/19575

pylori encoded polypeptide exhibits a *H. pylori* biological activity, e.g., the encoded *H. pylori* enzyme retains a biological activity of a naturally occurring *H. pylori*.

In preferred embodiments, the encoded polypeptide includes all or a fragment of an amino acid sequence of the invention contained in the Sequence Listing; fused, in reading frame, to additional amino acid residues, preferably to residues encoded by genomic DNA 5' or 3' to the genomic DNA which encodes a sequence of the invention contained in the Sequence Listing.

5

10

15

20

25

30

35

In preferred embodiments, the subject *H. pylori* nucleic acid will include a transcriptional regulatory sequence, e.g. at least one of a transcriptional promoter or transcriptional enhancer sequence, operably linked to the *H. pylori* gene sequence, e.g., to render the *H. pylori* gene sequence suitable for expression in a recombinant host cell.

In yet a further preferred embodiment, the nucleic acid which encodes an *H. pylori* polypeptide of the invention, hybridizes under stringent conditions to a nucleic acid probe corresponding to at least 8 consecutive nucleotides of the invention contained in the Sequence Listing; more preferably to at least 12 consecutive nucleotides of the invention contained in the Sequence Listing; more preferably to at least 20 consecutive nucleotides of the invention contained in the Sequence Listing; more preferably to at least 40 consecutive nucleotides of the invention contained in the Sequence Listing.

In a preferred embodiment, the nucleic acid encodes a peptide which differs by at least one amino acid residue from the sequences of the invention contained in the Sequence Listing.

In a preferred embodiment, the nucleic acid differs by at least one nucleotide from a nucleotide sequence of the invention contained in the Sequence Listing which encodes amino acids of the invention contained in the Sequence Listing.

In another aspect, the invention encompasses: a vector including a nucleic acid which encodes an *H. pylori* polypeptide or an *H. pylori* polypeptide variant as described herein; a host cell transfected with the vector; and a method of producing a recombinant *H. pylori* polypeptide or *H. pylori* polypeptide variant; including culturing the cell, e.g., in a cell culture medium, and isolating the *H. pylori* or *H. pylori* polypeptide variant, e.g., from the cell or from the cell culture medium.

In another aspect, the invention features, a purified recombinant nucleic acid having at least 50%, 60%, 70%, 80%, 90%, 95%, 98%, or 99% homology with a sequence of the invention contained in the Sequence Listing.

The invention also provides a probe or primer which includes a substantially purified oligonucleotide. The oligonucleotide includes a region of nucleotide sequence which hybridizes under stringent conditions to at least 8 consecutive nucleotides of sense or antisense sequence of the invention contained in the Sequence Listing, or

10

15

20

25

30

35

naturally occurring mutants thereof. In preferred embodiments, the probe or primer further includes a label group attached thereto. The label group can be, e.g., a radioisotope, a fluorescent compound, an enzyme, and/or an enzyme co-factor. Preferably the oligonucleotide is at least 8 and less than 10, 20, 30, 50, 100, or 150 nucleotides in length.

The invention also provides an isolated *H. pylori* polypeptide which is encoded by a nucleic acid which hybridizes under stringent hybridization conditions to a nucleic acid contained in the Sequence Listing.

The invention further provides nucleic acids, e.g., RNA or DNA, encoding a polypeptide of the invention. This includes double stranded nucleic acids as well as coding and antisense single strands.

The *H. pylori* strain, from which genomic sequences have been sequenced, has been deposited in the American Type Culture Collection (ATCC # 55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) as strain HP-J99.

Included in the invention are: allelic variations; natural mutants; induced mutants; proteins encoded by DNA that hybridizes under high or low stringency conditions to a nucleic acid which encodes a polypeptide of the invention contained in the Sequence Listing (for definitions of high and low stringency see Current Protocols in Molecular Biology, John Wiley & Sons, New York, 1989, 6.3.1 - 6.3.6 and 6.4.1-6.4.10, hereby incorporated by reference); and, polypeptides specifically bound by antisera to *H. pylori* polypeptides, especially by antisera to an active site or binding domain of *H. pylori* polypeptide. The invention also includes fragments, preferably biologically active fragments. These and other polypeptides are also referred to herein as *H. pylori* polypeptide analogs or variants.

Putative functions have been determined for several of the *H. pylori* polypeptides of the invention, as shown in Table 1.

Accordingly, uses of the claimed *H. pylori* polypeptides based on these identified functions, as well as other functions as described herein, are also within the scope of the invention.

In addition, the present invention encompasses *H. pylori* polypeptides characterized as shown in Table 1 below, including: *H. pylori* cell envelope proteins, *H. pylori* secreted proteins, and *H. pylori* cellular proteins. Members of these groups were identified by BLAST homology searches and by searches for secretion signal or transmembrane protein motifs. Polypeptides related by significant homology to the polypeptides of Table 1 are also considered to be classified in the manner of the homologs shown in Table 1.

TABLE 1

ORF_Name and Group	nt SeqID	aa Seq1D
A. CELL ENVELOPE		
A.1 Inner membrane proteins	<del> </del>	<del></del>
02ge11622_23494043_f1_6	3	76
hp5p15212_13095752_c3_36	25	
06ep30223_20173437_f1_37	48	
A.2 Outer membrane proteins	40	121
05ee10816_14495437_f2_13	10	83
	10	- 63
A.2.1 Terminal phe residue	40	
06ep11509_35954752_f2_1	16	
06ep10615_14495437_f3_47	45	
03ae10804_14495437_c2_38	35	
05ae30220_917200_c3_172	37	L
04cp11202_23646885_f2_26	7	L
05ep10815_16131925_c2_97	39	
09cp61003_5860877_f2_23	55	
09ae10512_48768_c3_67	18	<del></del>
09cp11003_5860877_f3_7	19	
hp6e12267_30478562_f3_33	28	
06cp30603_34174212_c3_71	30	
09cp10224_1962590_f3_31	52	
09cp61003_30478562_c3_106	54	127
11ae80818_10553192_f2_16	56	
11ee11408_10584582_c3_51	58	131
A.2.2 Terminal phe residue and C-		
terminal tyrosine cluster	<u> </u>	
01ae12001_116018_c2_40	1	
06ap10609_116018_c3_50	42	115
06cp30603_4687507_f1_9	14	
06cp30603_4687507_f1_7	43	116
05ee10816_36126938_f3_16	-11	84
01cp20708_4960952_c1_43	71	144
A.3 Via homolgy		
07ap80601_5083193_f3_8	. 17	90
11ap20714_4797137_f3_45	57	130
A.4 Other cell envelope proteins		
04ap12016_25501501_f1_1	5	78
04cp11202 20415937_f2_25	6	
04ee11108_3906963_f1_7	8	
29ep10720_25501501_c2_33	21	1
B. SECRETED PROTEINS	<del>                                     </del>	<del> </del>
hp3e10342_22448587_c2_15	72	145
	32	
hp5p15212_24276587_f1_2	51	1
09ce10413_35336707_f2_9	1 21	1 124

01ae12001_32462543_c2_43	2	75
03ee11215_1416312_c3_35	4	
05ae30220_14570443_c2_94	9	
06cp30603_2772578_c1_46	13	
29ep10720_289077_f2_12	22	
03ee11215_22542803 f1 7	29	
09ae10512_3166040_c1_40	31	102 104
01ce11104_10742963 c2 12	33	
02ge10116_36335436_f3_66	33	106
04ep41903_11876461_f1_4	<del></del>	107
05ce10208_23631292_f1_6	36	109
05ep10815_22447252_c3_110	38	111
05ep10815_30283516 c3 109	40	113
06ee30709_33851038_c3_30	41	114
06ep11202_21687842_c3_35	44	117
06ep30223_2774062_f1_33	46	119
09cp10713_23912707_c1_26	49	122
11ee11408_4882318_f3_24	53	126
hp4e13394_5908553 ft 1	59	132
hp4e13394_390633_11_1 hp4e53394_1416312_c3_119	61	134
hp5e15211_24328910_c3_38	62	135
hp6p10606_23493756_c1_21	63	136
hp6p22217_23564012_f1_5	65	138
hp6p22217_23364012_11_5	66	139
hp6p22217_2922143 f2 9	67	140
C. OTHER CELLULAR PROTEINS	68	141
06ap11119_14726542_f3_21		
06ee10709_6136430_c1 11	12	85
12ap10605_14094816_c1_5	15	88
hp2p10272_34042518_f1_2	20	93
hp5e15211_25411557_c1_22	23	96
	24	97
hp5p15641_3907968_f1_3 hp6e10967_657638_f3_9	26	99
06ep11202_4569693_c2_28	27	100
06ep30223_3930468_c1 110	47	120
	50	123
hp2e10911_960952_c2_86	60	133
hp6p10509_14642217_c2_17	64	137
hp6p80503_20964382_f2_11	69	142
hp7e10192_5917593_f1_2	70	143
hp6p10509_14642217_c3_25	73	146

[In Table 1, "nt" represents nucleotide Seq. ID number and "aa" represents amino acid Seq. ID number]

### 5 <u>Definitions</u>

The terms "purified polypeptide" and "isolated polypeptide" and "a substantially pure preparation of a polypeptide" are used interchangeably herein and, as used herein,

WO 98/18323 PCT/US97/19575

from other proteins, lipids, and nucleic acids with which it naturally occurs. Preferably, the polypeptide is also separated from substances, e.g., antibodies or gel matrix, e.g., polyacrylamide, which are used to purify it. Preferably, the polypeptide constitutes at least 10, 20, 50 70, 80 or 95% dry weight of the purified preparation. Preferably, the preparation contains: sufficient polypeptide to allow protein sequencing; at least 1, 10, or 100 µg of the polypeptide; at least 1, 10, or 100 mg of the polypeptide. Furthermore, the terms "purified polypeptide" and "isolated polypeptide" and "a substantially pure preparation of a polypeptide," as used herein, refer to both a polypeptide obtained from nature or produced by recombinant DNA techniques as described herein.

10

15

20

5

For example, an "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the H. pylori protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of H. pylori protein in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. In one embodiment, the language "substantially free of cellular material" includes preparations of H. pylori protein having less than about 30% (by dry weight) of non-H. pylori protein (also referred to herein as a "contaminating protein"), more preferably less than about 20% of non-H. pylori protein, still more preferably less than about 10% of non-H. pylori protein, and most preferably less than about 5% non-H. pylori protein. When the H. pylori protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the protein preparation.

25

30

The language "substantially free of chemical precursors or other chemicals" includes preparations of *H. pylori* protein in which the protein is separated from chemical precusors or other chemicals which are involved in the synthesis of the protein. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of *H. pylori* protein having less than about 30% (by dry weight) of chemical precursors or non-*H. pylori* chemicals, more preferably less than about 20% chemical precursors or non-*H. pylori* chemicals, still more preferably less than about 10% chemical precursors or non-*H. pylori* chemicals, and most preferably less than about 5% chemical precursors or non-*H. pylori* chemicals.

35

A purified preparation of cells refers to, in the case of plant or animal cells, an *in* vitro preparation of cells and not an entire intact plant or animal. In the case of cultured

10

15

20

25

30

35

cells or microbial cells, it consists of a preparation of at least 10% and more preferably 50% of the subject cells.

A purified or isolated or a substantially pure nucleic acid, e.g., a substantially pure DNA, (are terms used interchangeably herein) is a nucleic acid which is one or both of the following: not immediately contiguous with both of the coding sequences with which it is immediately contiguous (i.e., one at the 5' end and one at the 3' end) in the naturally-occurring genome of the organism from which the nucleic acid is derived; or which is substantially free of a nucleic acid with which it occurs in the organism from which the nucleic acid is derived. The term includes, for example, a recombinant DNA which is incorporated into a vector, e.g., into an autonomously replicating plasmid or virus, or into the genomic DNA of a prokaryote or eukaryote, or which exists as a separate molecule (e.g., a cDNA or a genomic DNA fragment produced by PCR or restriction endonuclease treatment) independent of other DNA sequences. Substantially pure DNA also includes a recombinant DNA which is part of a hybrid gene encoding additional *H. pylori* DNA sequence.

A "contig" as used herein is a nucleic acid representing a continuous stretch of genomic sequence of an organism.

An "open reading frame", also referred to herein as ORF, is a region of nucleic acid which encodes a polypeptide. This region may represent a portion of a coding sequence or a total sequence and can be determined from a stop to stop codon or from a start to stop codon.

As used herein, a "coding sequence" is a nucleic acid which is transcribed into messenger RNA and/or translated into a polypeptide when placed under the control of appropriate regulatory sequences. The boundaries of the coding sequence are determined by a translation start codon at the five prime terminus and a translation stop code at the three prime terminus. A coding sequence can include but is not limited to messenger RNA, synthetic DNA, and recombinant nucleic acid sequences.

A "complement" of a nucleic acid as used herein referes to an anti-parallel or antisense sequence that participates in Watson-Crick base-pairing with the original sequence.

A "gene product" is a protein or structural RNA which is specifically encoded by a gene.

As used herein, the term "probe" refers to a nucleic acid, peptide or other chemical entity which specifically binds to a molecule of interest. Probes are often associated with or capable of associating with a label. A label is a chemical moiety capable of detection. Typical labels comprise dyes, radioisotopes, luminescent and chemiluminescent moieties, fluorophores, enzymes, precipitating agents, amplification

10

15

20

25.

30

35

sequences, and the like. Similarly, a nucleic acid, peptide or other chemical entity which specifically binds to a molecule of interest and immobilizes such molecule is referred herein as a "capture ligand". Capture ligands are typically associated with or capable of associating with a support such as nitro-cellulose, glass, nylon membranes, beads, particles and the like. The specificity of hybridization is dependent on conditions such as the base pair composition of the nucleotides, and the temperature and salt concentration of the reaction. These conditions are readily discernable to one of ordinary skill in the art using routine experimentation.

Homologous refers to the sequence similarity or sequence identity between two polypeptides or between two nucleic acid molecules. When a position in both of the two compared sequences is occupied by the same base or amino acid monomer subunit, e.g., if a position in each of two DNA molecules is occupied by adenine, then the molecules are homologous at that position. The percent of homology between two sequences is a function of the number of matching or homologous positions shared by the two sequences divided by the number of positions compared x 100. For example, if 6 of 10 of the positions in two sequences are matched or homologous then the two sequences are 60% homologous. By way of example, the DNA sequences ATTGCC and TATGGC share 50% homology. Generally, a comparison is made when two sequences are aligned to give maximum homology.

Nucleic acids are hybridizable to each other when at least one strand of a nucleic acid can anneal to the other nucleic acid under defined stringency conditions.

Stringency of hybridization is determined by: (a) the temperature at which hybridization and/or washing is performed; and (b) the ionic strength and polarity of the hybridization and washing solutions. Hybridization requires that the two nucleic acids contain complementary sequences; depending on the stringency of hybridization, however, mismatches may be tolerated. Typically, hybridization of two sequences at high stingency (such as, for example, in a solution of 0.5X SSC, at 65° C) requires that the sequences be essentially completely homologous. Conditions of intermediate stringency (such as, for example, 2X SSC at 65° C) and low stringency (such as, for example 2X SSC at 55° C), require correspondingly less overall complementarity between the hybridizing sequences. (1X SSC is 0.15 M NaCl, 0.015 M Na citrate). A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65°C.

The terms peptides, proteins, and polypeptides are used interchangeably herein.

10

15

20

25

30

35

As used herein, the term "surface protein" refers to all surface accessible proteins, e.g. inner and outer membrane proteins, proteins adhering to the cell wall, and secreted proteins.

A polypeptide has *H. pylori* biological activity if it has one, two and preferably more of the following properties: (1) if when expressed in the course of an *H. pylori* infection, it can promote, or mediate the attachment of *H. pylori* to a cell; (2) it has an enzymatic activity, structural or regulatory function characteristic of an *H. pylori* protein; (3) the gene which encodes it can rescue a lethal mutation in an *H. pylori* gene; (4) or it is immunogenic in a subject. A polypeptide has biological activity if it is an antagonist, agonist, or super-agonist of a polypeptide having one of the above-listed properties.

A biologically active fragment or analog is one having an *in vivo* or *in vitro* activity which is characteristic of the *H. pylori* polypeptides of the invention contained in the Sequence Listing, or of other naturally occurring *H. pylori* polypeptides, e.g., one or more of the biological activities described herein. Especially preferred are fragments which exist *in vivo*, e.g., fragments which arise from post transcriptional processing or which arise from translation of alternatively spliced RNA's. Fragments include those expressed in native or endogenous cells as well as those made in expression systems, e.g., in CHO cells. Because peptides such as *H. pylori* polypeptides often exhibit a range of physiological properties and because such properties may be attributable to different portions of the molecule, a useful *H. pylori* fragment or *H. pylori* analog is one which exhibits a biological activity in any biological assay for *H. pylori* activity. Most preferably the fragment or analog possesses 10%, preferably 40%, more preferably 60%, 70%, 80% or 90% or greater of the activity of *H. pylori*, in any *in vivo* or *in vitro* assay.

Analogs can differ from naturally occurring *H. pylori* polypeptides in amino acid sequence or in ways that do not involve sequence, or both. Non-sequence modifications include changes in acetylation, methylation, phosphorylation, carboxylation, or glycosylation. Preferred analogs include *H. pylori* polypeptides (or biologically active fragments thereof) whose sequences differ from the wild-type sequence by one or more conservative amino acid substitutions or by one or more non-conservative amino acid substitutions, deletions, or insertions which do not substantially diminish the biological activity of the *H. pylori* polypeptide. Conservative substitutions typically include the substitution of one amino acid for another with similar characteristics, e.g., substitutions within the following groups: valine, glycine; glycine, alanine; valine, isoleucine, leucine; aspartic acid, glutamic acid; asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine. Other conservative substitutions can be made in view of the table below.

TABLE 2
CONSERVATIVE AMINO ACID REPLACEMENTS

For Amino Acid	Code	Replace with any of
Alanine	A	D-Ala, Gly, beta-Ala, L-Cys, D-Cys
Arginine	R	D-Arg, Lys, D-Lys, homo-Arg, D-homo-Arg, Met, Ile,
	· .	D-Met, D-Ile, Orn, D-Orn
Asparagine	N	D-Asn, Asp, D-Asp, Glu, D-Glu, Gln, D-Gln
Aspartic Acid	D	D-Asp, D-Asn, Asn, Glu, D-Glu, Gln, D-Gln
Cysteine	C .	D-Cys, S-Me-Cys, Met, D-Met, Thr, D-Thr
Glutamine	Q	D-Gln, Asn. D-Asn, Glu, D-Glu, Asp, D-Asp
Glutamic Acid	E	D-Glu, D-Asp, Asp, Asn, D-Asn, Gln, D-Gln
Glycine	G	Ala, D-Ala, Pro, D-Pro, β-Ala, Acp
Isoleucine	I	D-Ile, Val, D-Val, Leu, D-Leu, Met, D-Met
Leucine	L .	D-Leu, Val, D-Val, Leu, D-Leu, Met, D-Met
Lysine	K	D-Lys, Arg, D-Arg, homo-Arg, D-homo-Arg, Met, D-
		Met, Ile, D-Ile, Orn, D-Orn
Methionine	М	D-Met, S-Me-Cys, Ile, D-Ile, Leu, D-Leu, Val, D-Val
Phenylalanine	F	D-Phe, Tyr, D-Thr, L-Dopa, His, D-His, Trp, D-Trp,
		Trans-3,4, or 5-phenylproline, cis-3,4,
		or 5-phenylproline
Proline	P	D-Pro, L-I-thioazolidine-4-carboxylic acid, D-or L-1-
·		oxazolidine-4-carboxylic acid
Serine	S	D-Ser, Thr, D-Thr, allo-Thr, Met, D-Met, Met(O),
	ů.	D-Met(O), L-Cys, D-Cys
Threonine	Т	D-Thr, Ser, D-Ser, allo-Thr, Met, D-Met, Met(O),
		D-Met(O), Val, D-Val
Tyrosine	Y	D-Tyr, Phe, D-Phe, L-Dopa, His, D-His
Valine	V	D-Val, Leu, D-Leu, Ile, D-Ile, Met, D-Met

10

15

20

25

30

35

Other analogs within the invention are those with modifications which increase peptide stability; such analogs may contain, for example, one or more non-peptide bonds (which replace the peptide bonds) in the peptide sequence. Also included are: analogs that include residues other than naturally occurring L-amino acids, e.g., D-amino acids or non-naturally occurring or synthetic amino acids, e.g.,  $\beta$  or  $\gamma$  amino acids; and cyclic analogs.

As used herein, the term "fragment", as applied to an *H. pylori* analog, will ordinarily be at least about 20 residues, more typically at least about 40 residues, preferably at least about 60 residues in length. Fragments of *H. pylori* polypeptides can be generated by methods known to those skilled in the art. The ability of a candidate fragment to exhibit a biological activity of *H. pylori* polypeptide can be assessed by methods known to those skilled in the art as described herein. Also included are *H. pylori* polypeptides containing residues that are not required for biological activity of the peptide or that result from alternative mRNA splicing or alternative protein processing events.

An "immunogenic component" as used herein is a moiety, such as an *H. pylori* polypeptide, analog or fragment thereof, that is capable of eliciting a humoral and/or cellular immune response in a host animal alone or in combination with an adjuvant.

An "antigenic component" as used herein is a moiety, such as an *H. pylori* polypeptide, analog or fragment thereof, that is capable of binding to a specific antibody with sufficiently high affinity to form a detectable antigen-antibody complex.

As used herein, the term "transgene" means a nucleic acid (encoding, e.g., one or more polypeptides), which is partly or entirely heterologous, i.e., foreign, to the transgenic animal or cell into which it is introduced, or, is homologous to an endogenous gene of the transgenic animal or cell into which it is introduced, but which is designed to be inserted, or is inserted, into the cell's genome in such a way as to alter the genome of the cell into which it is inserted (e.g., it is inserted at a location which differs from that of the natural gene or its insertion results in a knockout). A transgene can include one or more transcriptional regulatory sequences and any other nucleic acid, such as introns, that may be necessary for optimal expression of the selected nucleic acid, all operably linked to the selected nucleic acid, and may include an enhancer sequence.

As used herein, the term "transgenic cell" refers to a cell containing a transgene. As used herein, a "transgenic animal" is any animal in which one or more, and preferably essentially all, of the cells of the animal includes a transgene. The transgene can be introduced into the cell, directly or indirectly by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by a process of transformation of competent cells or by microinjection or by infection with a

10

15

20

25

30 .

35

recombinant virus. This molecule may be integrated within a chromosome, or it may be extrachromosomally replicating DNA.

The term "antibody" as used herein is intended to include fragments thereof which are specifically reactive with *H. pylori* polypeptides.

As used herein, the term "cell-specific promoter" means a DNA sequence that serves as a promoter, i.e., regulates expression of a selected DNA sequence operably linked to the promoter, and which effects expression of the selected DNA sequence in specific cells of a tissue. The term also covers so-called "leaky" promoters, which regulate expression of a selected DNA primarily in one tissue, but cause expression in other tissues as well.

Misexpression, as used herein, refers to a non-wild type pattern of gene expression. It includes: expression at non-wild type levels, i.e., over or under expression; a pattern of expression that differs from wild type in terms of the time or stage at which the gene is expressed, e.g., increased or decreased expression (as compared with wild type) at a predetermined developmental period or stage; a pattern of expression that differs from wild type in terms of decreased expression (as compared with wild type) in a predetermined cell type or tissue type; a pattern of expression that differs from wild type in terms of the splicing size, amino acid sequence, post-transitional modification, or biological activity of the expressed polypeptide; a pattern of expression that differs from wild type in terms of the effect of an environmental stimulus or extracellular stimulus on expression of the gene, e.g., a pattern of increased or decreased expression (as compared with wild type) in the presence of an increase or decrease in the strength of the stimulus.

As used herein, "host cells" and other such terms denoting microorganisms or higher eukaryotic cell lines cultured as unicellular entities refers to cells which can become or have been used as recipients for a recombinant vector or other transfer DNA, and include the progeny of the original cell which has been transfected. It is understood by individuals skilled in the art that the progeny of a single parental cell may not necessarily be completely identical in genomic or total DNA compliment to the original parent, due to accident or deliberate mutation.

As used herein, the term "control sequence" refers to a nucleic acid having a base sequence which is recognized by the host organism to effect the expression of encoded sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism; in prokaryotes, such control sequences generally include a promoter, ribosomal binding site, terminators, and in some cases operators; in eukaryotes, generally such control sequences include promoters, terminators and in some instances, enhancers. The term control sequence is intended to include at a

10

15

20

25

30

35

minimum, all components whose presence is necessary for expression, and may also include additional components whose presence is advantageous, for example, leader sequences.

As used herein, the term "operably linked" refers to sequences joined or ligated to function in their intended manner. For example, a control sequence is operably linked to coding sequence by ligation in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequence and host cell.

The metabolism of a substance, as used herein, means any aspect of the, expression, function, action, or regulation of the substance. The metabolism of a substance includes modifications, e.g., covalent or non-covalent modifications of the substance. The metabolism of a substance includes modifications, e.g., covalent or non-covalent modification, the substance induces in other substances. The metabolism of a substance also includes changes in the distribution of the substance. The metabolism of a substance includes changes the substance induces in the distribution of other substances.

A "sample" as used herein refers to a biological sample, such as, for example, tissue or fluid isloated from an individual (including without limitation plasma, serum, cerebrospinal fluid, lymph, tears, saliva and tissue sections) or from *in vitro* cell culture constituents, as well as samples from the environment.

The practice of the invention will employ, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. See e.g., Sambrook, Fritsch, and Maniatis, Molecular Cloning; Laboratory Manual 2nd ed. (1989); DNA Cloning, Volumes I and II (D.N Glover ed. 1985); Oligonucleotide Synthesis (M.J. Gait ed, 1984); Nucleic Acid Hybridization (B.D. Hames & S.J. Higgins eds. 1984); the series, Methods in Enzymology (Academic Press, Inc.), particularly Vol. 154 and Vol. 155 (Wu and Grossman, eds.) and PCR-A Practical Approach (McPherson, Quirke, and Taylor, eds., 1991).

### I. Isolation of Nucleic Acids of H. pylori and Uses Therefor

### H. pylori Genomic Sequence

This invention provides nucleotide sequences of the genome of *H. pylori* which thus comprises a DNA sequence library of *H. pylori* genomic DNA. The detailed description that follows provides nucleotide sequences of *H. pylori*, and also describes how the sequences were obtained and how ORFs and protein-coding sequences were

WO 98/18323 PCT/US97/19575

identified. Also described are methods of using the disclosed *H. pylori* sequences in methods including diagnostic and therapeutic applications. Furthermore, the library can be used as a database for identification and comparison of medically important sequences in this and other strains of *H. pylori*.

5

10

15

20

25

30

35

To determine the genomic sequence of *H. pylori*, DNA was isolated from a strain of *H. pylori* (ATCC # 55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) and mechanically sheared by nebulization to a median size of 2 kb. Following size fractionation by gel electrophoresis, the fragments were blunt-ended, ligated to adapter oligonucleotides, and cloned into each of 20 different pMPX vectors (Rice et al., abstracts of Meeting of Genome Mapping and Sequencing, Cold Spring Harbor, NY, 5/11-5/15, 1994, p. 225) to construct a series of "shotgun" subclone libraries.

DNA sequencing was achieved using multiplex sequencing procedures essentially as disclosed in Church et al., 1988, *Science* 240:185; U.S. Patents No. 4,942,124 and 5,149,625). DNA was extracted from pooled cultures and subjected to chemical or enzymatic sequencing. Sequencing reactions were resolved by electrophoresis, and the products were transferred and covalently bound to nylon membranes. Finally, the membranes were sequentially hybridized with a series of labelled oligonucleotides complimentary to "tag" sequences present in the different shotgun cloning vectors. In this manner, a large number of sequences could be obtained from a single set of sequencing reactions. The cloning and sequencing procedures are described in more detail in the Exemplification.

Individual sequence reads obtained in this manner were assembled using the FALCON<sup>TM</sup> program (Church *et al.*, 1994, *Automated DNA Sequencing and Analysis*, J.C. Venter, ed., Academic Press) and PHRAP (P. Green, Abstracts of DOE Human Genome Program Contractor-Grantee Workshop V, Jan. 1996, p.157). The average contig length was about 3-4 kb.

A variety of approaches are used to order the contigs so as to obtain a continuous sequence representing the entire *H. pylori* genome. Synthetic oligonucleotides are designed that are complementary to sequences at the end of each contig. These oligonucleotides may be hybridized to libaries of *H. pylori* genomic DNA in, for example, lambda phage vectors or plasmid vectors to identify clones that contain sequences corresponding to the junctional regions between individual contigs. Such clones are then used to isolate template DNA and the same oligonucleotides are used as primers in polymerase chain reaction (PCR) to amplify junctional fragments, the nucleotide sequence of which is then determined.

10

20

25

30

35

The *H. pylori* sequences were analyzed for the presence of open reading frames (ORFs) comprising at least 180 nucleotides. As a result of the analysis of ORFs based on stop-to-stop codon reads, it should be understood that these ORFs may not correspond to the ORF of a naturally-occurring *H. pylori* polypeptide. These ORFs may contain start codons which indicate the initiation of protein synthesis of a naturally-occurring *H. pylori* polypeptide. Such start codons within the ORFs provided herein can be identified by those of ordinary skill in the relevant art, and the resulting ORF and the encoded *H. pylori* polypeptide is within the scope of this invention. For example, within the ORFs a codon such as AUG or GUG (encoding methionine or valine) which is part of the initiation signal for protein synthesis can be identified and the ORF modified to correspond to a naturally-occurring *H. pylori* polypeptide. The predicted coding regions were defined by evaluating the coding potential of such sequences with the program GENEMARK<sup>TM</sup> (Borodovsky and McIninch, 1993, *Comp. Chem.* 17:123).

### 15 Other H. pylori Nucleic Acids

The nucleic acids of this invention may be obtained directly from the DNA of the above referenced *H. pylori* strain by using the polymerase chain reaction (PCR). See "PCR, A Practical Approach" (McPherson, Quirke, and Taylor, eds., IRL Press, Oxford, UK, 1991) for details about the PCR. High fidelity PCR can be used to ensure a faithful DNA copy prior to expression. In addition, the authenticity of amplified products can be checked by conventional sequencing methods. Clones carrying the desired sequences described in this invention may also be obtained by screening the libraries by means of the PCR or by hybridization of synthetic oligonucleotide probes to filter lifts of the library colonies or plaques as known in the art (see, e.g., Sambrook et al., Molecular Cloning, A Laboratory Manual 2nd edition, 1989, Cold Spring Harbor Press, NY).

It is also possible to obtain nucleic acids encoding *H. pylori* polypeptides from a cDNA library in accordance with protocols herein described. A cDNA encoding an *H. pylori* polypeptide can be obtained by isolating total mRNA from an appropriate strain. Double stranded cDNAs can then be prepared from the total mRNA. Subsequently, the cDNAs can be inserted into a suitable plasmid or viral (e.g., bacteriophage) vector using any one of a number of known techniques. Genes encoding *H. pylori* polypeptides can also be cloned using established polymerase chain reaction techniques in accordance with the nucleotide sequence information provided by the invention. The nucleic acids of the invention can be DNA or RNA. Preferred nucleic acids of the invention are contained in the Sequence Listing.

The nucleic acids of the invention can also be chemically synthesized using standard techniques. Various methods of chemically synthesizing polydeoxynucleotides

WO 98/18323

PCT/US97/19575

are known, including solid-phase synthesis which, like peptide synthesis, has been fully automated in commercially available DNA synthesizers (See e.g., Itakura et al. U.S. Patent No. 4,598,049; Caruthers et al. U.S. Patent No. 4,458,066; and Itakura U.S. Patent Nos. 4,401,796 and 4,373,071, incorporated by reference herein).

Nucleic acids isolated or synthesized in accordance with features of the present invention are useful, by way of example, without limitation, as probes, primers, capture ligands, antisense genes and for developing expression systems for the synthesis of proteins and peptides corresponding to such sequences. As probes, primers, capture ligands and antisense agents, the nucleic acid normally consists of all or part (approximately twenty or more nucleotides for specificity as well as the ability to form stable hybridization products) of the nucleic acids of the invention contained in the Sequence Listing. These uses are described in further detail below.

#### **Probes**

5

10

15

20

25

30

35

A nucleic acid isolated or synthesized in accordance with the sequence of the invention contained in the Sequence Listing can be used as a probe to specifically detect *H. pylori*. With the sequence information set forth in the present application, sequences of twenty or more nucleotides are identified which provide the desired inclusivity and exclusivity with respect to *H. pylori*, and extraneous nucleic acids likely to be encountered during hybridization conditions. More preferably, the sequence will comprise at least twenty to thirty nucleotides to convey stability to the hybridization product formed between the probe and the intended target molecules.

Sequences larger than 1000 nucleotides in length are difficult to synthesize but can be generated by recombinant DNA techniques. Individuals skilled in the art will readily recognize that the nucleic acids, for use as probes, can be provided with a label to facilitate detection of a hybridization product.

Nucleic acid isolated and synthesized in accordance with the sequence of the invention contained in the Sequence Listing can also be useful as probes to detect homologous regions (especially homologous genes) of other *Helicobacter* species using appropriate stringency hybridization conditions as described herein.

#### Capture Ligand

For use as a capture ligand, the nucleic acid selected in the manner described above with respect to probes, can be readily associated with a support. The manner in which nucleic acid is associated with supports is well known. Nucleic acid having twenty or more nucleotides in a sequence of the invention contained in the Sequence Listing have utility to separate *H. pylori* nucleic acid from the nucleic acid of each other and other organisms. Nucleic acid having twenty or more nucleotides in a sequence of the invention contained in the Sequence Listing can also have utility to separate other

10

15

20

25

30

Helicobacter species from each other and from other organisms. Preferably, the sequence will comprise at least twenty nucleotides to convey stability to the hybridization product formed between the probe and the intended target molecules. Sequences larger than 1000 nucleotides in length are difficult to synthesize but can be generated by recombinant DNA techniques.

#### **Primers**

Nucleic acid isolated or synthesized in accordance with the sequences described herein have utility as primers for the amplification of H. pylori nucleic acid. These nucleic acids may also have utility as primers for the amplification of nucleic acids in other Helicobacter species. With respect to polymerase chain reaction (PCR) techniques, nucleic acid sequences of  $\geq 10$ -15 nucleotides of the invention contained in the Sequence Listing have utility in conjunction with suitable enzymes and reagents to create copies of H. pylori nucleic acid. More preferably, the sequence will comprise twenty or more nucleotides to convey stability to the hybridization product formed between the primer and the intended target molecules. Binding conditions of primers greater than 100 nucleotides are more difficult to control to obtain specificity. High fidelity PCR can be used to ensure a faithful DNA copy prior to expression. In addition, amplified products can be checked by conventional sequencing methods.

The copies can be used in diagnostic assays to detect specific sequences, including genes from *H. pylori* and/or other *Helicobacter* species. The copies can also be incorporated into cloning and expression vectors to generate polypeptides corresponding to the nucleic acid synthesized by PCR, as is described in greater detail herein.

#### <u>Antisense</u>

Nucleic acid or nucleic acid-hybridizing derivatives isolated or synthesized in accordance with the sequences described herein have utility as antisense agents to prevent the expression of *H. pylori* genes. These sequences also have utility as antisense agents to prevent expression of genes of other *Helicobacter* species.

In one embodiment, nucleic acid or derivatives corresponding to *H. pylori* nucleic acids is loaded into a suitable carrier such as a liposome or bacteriophage for introduction into bacterial cells. For example, a nucleic acid having twenty or more nucleotides is capable of binding to bacteria nucleic acid or bacteria messenger RNA. Preferably, the antisense nucleic acid is comprised of 20 or more nucleotides to provide necessary stability of a hybridization product of non-naturally occurring nucleic acid and bacterial nucleic acid and/or bacterial messenger RNA. Nucleic acid having a sequence greater than 1000 nucleotides in length is difficult to synthesize but can be generated by recombinant DNA techniques. Methods for loading antisense nucleic acid in liposomes

10

15

20

25

30

35

is known in the art as exemplified by U.S. Patent 4,241,046 issued December 23, 1980 to Papahadjopoulos et al.

### II. Expression of H. pylori Nucleic Acids

Nucleic acid isolated or synthesized in accordance with the sequences described herein have utility to generate polypeptides. The nucleic acid of the invention exemplified in the Sequence Listing or fragments of said nucleic acid encoding active portions of *H. pylori* polypeptides can be cloned into suitable vectors or used to isolate nucleic acid. The isolated nucleic acid is combined with suitable DNA linkers and cloned into a suitable vector.

The function of a specific gene or operon can be ascertained by expression in a bacterial strain under conditions where the activity of the gene product(s) specified by the gene or operon in question can be specifically measured. Alternatively, a gene product may be produced in large quantities in an expressing strain for use as an antigen, an industrial reagent, for structural studies, etc. This expression can be accomplished in a mutant strain which lacks the activity of the gene to be tested, or in a strain that does not produce the same gene product(s). This includes, but is not limited to other Helicobacter strains, or other bacterial strains such as E. coli, Norcardia, Corynebacterium, Campylobacter, and Streptomyces species. In some cases the expression host will utilize the natural Helicobacter promoter whereas in others, it will be necessary to drive the gene with a promoter sequence derived from the expressing organism (e.g., an E. coli beta-galactosidase promoter for expression in E. coli).

To express a gene product using the natural *H. pylori* promoter, a procedure such as the following can be used. A restriction fragment containing the gene of interest, together with its associated natural promoter element and regulatory sequences (identified using the DNA sequence data) is cloned into an appropriate recombinant plasmid containing an origin of replication that functions in the host organism and an appropriate selectable marker. This can be accomplished by a number of procedures known to those skilled in the art. It is most preferably done by cutting the plasmid and the fragment to be cloned with the same restriction enzyme to produce compatible ends that can be ligated to join the two pieces together. The recombinant plasmid is introduced into the host organism by, for example, electroporation and cells containing the recombinant plasmid are identified by selection for the marker on the plasmid. Expression of the desired gene product is detected using an assay specific for that gene product.

In the case of a gene that requires a different promoter, the body of the gene (coding sequence) is specifically excised and cloned into an appropriate expression

30

35

plasmid. This subcloning can be done by several methods, but is most easily accomplished by PCR amplification of a specific fragment and ligation into an expression plasmid after treating the PCR product with a restriction enzyme or exonuclease to create suitable ends for cloning.

A suitable host cell for expression of a gene can be any procaryotic or eucaryotic cell. For example, an *H. pylori* polypeptide can be expressed in bacterial cells such as *E. coli*, insect cells (baculovirus), yeast, or mammalian cells such as Chinese hamster ovary cell (CHO). Other suitable host cells are known to those skilled in the art.

Expression in eucaryotic cells such as mammalian, yeast, or insect cells can lead to partial or complete glycosylation and/or formation of relevant inter- or intra-chain 10 disulfide bonds of a recombinant peptide product. Examples of vectors for expression in yeast S. cerivisae include pYepSec1 (Baldari. et al., (1987) Embo J. 6:229-234), pMFa (Kurjan and Herskowitz, (1982) Cell 30:933-943), pJRY88 (Schultz et al., (1987) Gene 54:113-123), and pYES2 (Invitrogen Corporation, San Diego, CA). Baculovirus vectors available for expression of proteins in cultured insect cells (SF 9 cells) include the pAc 15 series (Smith et al., (1983) Mol. Cell Biol. 3:2156-2165) and the pVL series (Lucklow, V.A., and Summers, M.D., (1989) Virology 170:31-39). Generally, COS cells (Gluzman, Y., (1981) Cell 23:175-182) are used in conjunction with such vectors as pCDM 8 (Aruffo, A. and Seed, B., (1987) Proc. Natl. Acad. Sci. USA 84:8573-8577) for transient amplification/expression in mammalian cells, while CHO (dhfr- Chinese 20 Hamster Ovary) cells are used with vectors such as pMT2PC (Kaufman et al. (1987), EMBO J. 6:187-195) for stable amplification/expression in mammalian cells. Vector DNA can be introduced into mammalian cells via conventional techniques such as calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, or electroporation. Suitable methods for transforming host cells can be 25 found in Sambrook et al. (Molecular Cloning: A Laboratory Manual, 2nd Edition, Cold Spring Harbor Laboratory press (1989)), and other laboratory textbooks.

Expression in procaryotes is most often carried out in *E. coli* with either fusion or non-fusion inducible expression vectors. Fusion vectors usually add a number of NH<sub>2</sub> terminal amino acids to the expressed target gene. These NH<sub>2</sub> terminal amino acids often are referred to as a reporter group. Such reporter groups usually serve two purposes: 1) to increase the solubility of the target recombinant protein; and 2) to aid in the purification of the target recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the reporter group and the target recombinant protein to enable separation of the target recombinant protein from the reporter group subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition

10

15

20

25

30

35

sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Amrad Corp., Melbourne, Australia), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase, maltose E binding protein, or protein A, respectively, to the target recombinant protein. A preferred reporter group is poly(His), which may be fused to the amino or carboxy terminus of the protein and which renders the recombinant fusion protein easily purifiable by metal chelate chromatography.

Inducible non-fusion expression vectors include pTrc (Amann et al., (1988) Gene 69:301-315) and pET11d (Studier et al., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 60-89). While target gene expression relies on host RNA polymerase transcription from the hybrid trp-lac fusion promoter in pTrc, expression of target genes inserted into pET11d relies on transcription from the T7 gn10-lac 0 fusion promoter mediated by coexpressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident λ prophage harboring a T7 gn1 under the transcriptional control of the lacUV 5 promoter.

For example, a host cell transfected with a nucleic acid vector directing expression of a nucleotide sequence encoding an *H. pylori* polypeptide can be cultured under appropriate conditions to allow expression of the polypeptide to occur. The polypeptide may be secreted and isolated from a mixture of cells and medium containing the peptide. Alternatively, the polypeptide may be retained cytoplasmically and the cells harvested, lysed and the protein isolated. A cell culture includes host cells, media and other byproducts. Suitable media for cell culture are well known in the art. Polypeptides of the invention can be isolated from cell culture medium, host cells, or both using techniques known in the art for purifying proteins including ion-exchange chromatography, gel filtration chromatography, ultrafiltration, electrophoresis, and immunoaffinity purification with antibodies specific for such polypeptides. Additionally, in many situations, polypeptides can be produced by chemical cleavage of a native protein (e.g., tryptic digestion) and the cleavage products can then be purified by standard techniques.

In the case of membrane bound proteins, these can be isolated from a host cell by contacting a membrane-associated protein fraction with a detergent forming a solubilized complex, where the membrane-associated protein is no longer entirely embedded in the membrane fraction and is solubilized at least to an extent which allows it to be chromatographically isolated from the membrane fraction. Several different criteria are used for choosing a detergent suitable for solubilizing these complexes. For example, one property considered is the ability of the detergent to solubilize the H.

10

15

20

25

30

pylori protein within the membrane fraction at minimal denaturation of the membraneassociated protein allowing for the activity or functionality of the membrane-associated protein to return upon reconstitution of the protein. Another property considered when selecting the detergent is the critical micelle concentration (CMC) of the detergent in that the detergent of choice preferably has a high CMC value allowing for ease of removal after reconstitution. A third property considered when selecting a detergent is the hydrophobicity of the detergent. Typically, membrane-associated proteins are very hydrophobic and therefore detergents which are also hydrophobic, e.g., the triton series, would be useful for solubilizing the hydrophobic proteins. Another property important to a detergent can be the capability of the detergent to remove the H. pylori protein with minimal protein-protein interaction facilitating further purification. A fifth property of the detergent which should be considered is the charge of the detergent. For example, if it is desired to use ion exchange resins in the purification process then preferably detergent should be an uncharged detergent. Chromatographic techniques which can be used in the final purification step are known in the art and include hydrophobic interaction, lectin affinity, ion exchange, dye affinity and immunoaffinity.

One strategy to maximize recombinant *H. pylori* peptide expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, S., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 119-128). Another strategy would be to alter the nucleic acid encoding an *H. pylori* peptide to be inserted into an expression vector so that the individual codons for each amino acid would be those preferentially utilized in highly expressed *E. coli* proteins (Wada et al., (1992) *Nuc. Acids Res.* 20:2111-2118). Such alteration of nucleic acids of the invention can be carried out by standard DNA synthesis techniques.

The nucleic acids of the invention can also be chemically synthesized using standard techniques. Various methods of chemically synthesizing polydeoxynucleotides are known, including solid-phase synthesis which, like peptide synthesis, has been fully automated in commercially available DNA synthesizers (See, e.g., Itakura et al. U.S. Patent No. 4,598,049; Caruthers et al. U.S. Patent No. 4,458,066; and Itakura U.S. Patent Nos. 4,401,796 and 4,373,071, incorporated by reference herein).

### III. H. pylori Polypeptides

This invention encompasses isolated *H. pylori* polypeptides encoded by the disclosed *H. pylori* genomic sequences, including the polypeptides of the invention contained in the Sequence Listing. Polypeptides of the invention are preferably at least 5 amino acid residues in length. Using the DNA sequence information provided herein,

15

20

25

30

35

the amino acid sequences of the polypeptides encompassed by the invention can be deduced using methods well-known in the art. It will be understood that the sequence of an entire nucleic acid encoding an *H. pylori* polypeptide can be isolated and identified based on an ORF that encodes only a fragment of the cognate protein-coding region. This can be acheived, for example, by using the isolated nucleic acid encoding the ORF, or fragments thereof, to prime a polymerase chain reaction with genomic *H. pylori* DNA as template; this is followed by sequencing the amplified product.

The polypeptides of the invention can be isolated from wild-type or mutant *H. pylori* cells or from heterologous organisms or cells (including, but not limited to, bacteria, yeast, insect, plant and mammalian cells) into which an *H. pylori* nucleic acid has been introduced and expressed. In addition, the polypeptides can be part of recombinant fusion proteins.

*H. pylori* polypeptides of the invention can be chemically synthesized using commercially automated procedures such as those referenced herein.

IV. Identification of Nucleic Acids Encoding Vaccine Components and Targets for Agents Effective Against H. pylori

The disclosed *H. pylori* genome sequence includes segments that direct the synthesis of ribonucleic acids and polypeptides, as well as origins of replication, promoters, other types of regulatory sequences, and intergenic nucleic acids. The invention encompasses nucleic acids encoding immunogenic components of vaccines and targets for agents effective against *H. pylori*. Identification of said immunogenic components involved in the determination of the function of the disclosed sequences can be achieved using a variety of approaches. Non-limiting examples of these approaches are described briefly below.

Homology to known sequences: Computer-assisted comparison of the disclosed *H. pylori* sequences with previously reported sequences present in publicly available databases is useful for identifying functional *H. pylori* nucleic acid and polypeptide sequences. It will be understood that protein-coding sequences, for example, may be compared as a whole, and that a high degree of sequence homology between two proteins (such as, for example, >80-90%) at the amino acid level indicates that the two proteins also possess some degree of functional homology, such as, for example, among enzymes involved in metabolism, DNA synthesis, or cell wall synthesis, and proteins involved in transport, cell division, etc. In addition, many structural features of particular protein classes have been identified and correlate with specific consensus sequences, such as, for example, binding domains for nucleotides, DNA, metal ions, and other small molecules; sites for covalent modifications such as phosphorylation,

10

15

20

25

30

35

acylation, and the like; sites of protein:protein interactions, etc. These consensus sequences may be quite short and thus may represent only a fraction of the entire protein-coding sequence. Identification of such a feature in an *H. pylori* sequence is therefore useful in determining the function of the encoded protein and identifying useful targets of antibacterial drugs.

Of particular relevance to the present invention are structural features that are common to secretory, transmembrane, and surface proteins, including secretion signal peptides and hydrophobic transmembrane domains. *H. pylori* proteins identified as containing putative signal sequences and/or transmembrane domains are useful as immunogenic components of vaccines.

Identification of essential genes: Nucleic acids that encode proteins essential for growth or viability of *H. pylori* are preferred drug targets. *H. pylori* genes can be tested for their biological relevance to the organism by examining the effect of deleting and/or disrupting the genes, i.e., by so-called gene "knockout", using techniques known to those skilled in the relevant art. In this manner, essential genes may be identified.

Strain-specific sequences: Because of the evolutionary relationship between different *H. pylori* strains, it is believed that the presently disclosed *H. pylori* sequences are useful for identifying, and/or discriminating between, previously known and new *H. pylori* strains. It is believed that other *H. pylori* strains will exhibit at least 70% sequence homology with the presently disclosed sequence. Systematic and routine analyses of DNA sequences derived from samples containing *H. pylori* strains, and comparison with the present sequence allows for the identification of sequences that can be used to discriminate between strains, as well as those that are common to all *H. pylori* strains. In one embodiment, the invention provides nucleic acids, including probes, and peptide and polypeptide sequences that discriminate between different strains of *H. pylori*. Strain-specific components can also be identified functionally by their ability to elicit or react with antibodies that selectively recognize one or more *H. pylori* strains.

In another embodiment, the invention provides nucleic acids, including probes, and peptide and polypeptide sequences that are common to all *H. pylori* strains but are *not* found in other bacterial species.

# Specific Example: Determination Of Candidate Protein Antigens For Antibody And Vaccine Development

The selection of candidate protein antigens for vaccine development can be derived from the nucleic acids encoding *H. pylori* polypeptides. First, the ORF's can be analyzed for homology to other known exported or membrane proteins and analyzed using the discriminant analysis described by Klein, et al. (Klein, P., Kanehsia, M., and

10

15

20

25 -

30

35

DeLisi, C. (1985) *Biochimica et Biophysica Acta* 815, 468-476) for predicting exported and membrane proteins.

Homology searches can be performed using the BLAST algorithm contained in the Wisconsin Sequence Analysis Package (Genetics Computer Group, University Research Park, 575 Science Drive, Madison, WI 53711) to compare each predicted ORF amino acid sequence with all sequences found in the current GenBank, SWISS-PROT and PIR databases. BLAST searches for local alignments between the ORF and the databank sequences and reports a probability score which indicates the probability of finding this sequence by chance in the database. ORF's with significant homology (e.g. probabilities lower than 1x10-6 that the homology is only due to random chance) to membrane or exported proteins represent protein antigens for vaccine development. Possible functions can be provided to *H. pylori* genes based on sequence homology to genes cloned in other organisms.

Discriminant analysis (Klein, et al. supra) can be used to examine the ORF amino acid sequences. This algorithm uses the intrinsic information contained in the ORF amino acid sequence and compares it to information derived from the properties of known membrane and exported proteins. This comparison predicts which proteins will be exported, membrane associated or cytoplasmic. ORF amino acid sequences identified as exported or membrane associated by this algorithm are likely protein antigens for vaccine development.

Surface exposed outer membrane proteins are likely to represent the best antigens to provide a protective immune response against *H. pylori*. Among the algorithms that can be used to aid in prediction of these outer membrane proteins include the presence of an amphipathic beta-sheet region at their C-terminus. This region which has been detected in a large number of outer membrane proteins in Gram negative bacteria is often characterized by hydrophobic residues (Phe or Tyr) clustered at alternating positions from the C-terminus (e.g., see Figure 5, block F; Figure 7, block E). Importantly, these sequences have not been detected at the C-termini of periplasmic proteins, thus allowing preliminary distinction between these classes of proteins based on primary sequence data. This phenomenon has been reported previously by Struyve et al. (*J. Mol. Biol.* 218:141-148, 1991).

Also illustrated in Figure 5 are additional amino acid sequence motifs found in many outer membrane proteins of *H. pylori*. The amino acid sequence alignment in Figure 5 depicts portions of the sequence of five *H. pylori* proteins (depicted in the single letter amino acid code) labeled with their amino acid Sequence ID Numbers and shown N-terminal to C-terminal, left to right. Five or six distinct blocks (labeled A through E or F) of similar amino acid residues are found including the distinctive

10

15

20

hydrophobic residues (Phe or Tyr; F or Y according to the single letter code for amino acid residues) frequently found at positions near the C-terminus of outer membrane proteins. The presence of several shared motifs clearly establishes the similarity between members of this group of proteins.

Additional amino acid alignments for four outer membrane proteins isolated from *H. pylori* are depicted in Figure 6.

Outer membrane proteins isolated from *H. pylori* frequently share additional motifs as depicted for two proteins in Figure 7 which also share the C-terminal hydrophobic residues, and as depicted for two proteins in Figure 8 which do not share the C-terminal hydrophobic residue motif but share a different C-terminal motif.

One skilled in the art would know that these shared sequence motifs are highly significant and establish a similarity among this group of proteins.

Infrequently it is not possible to distinguish between multiple possible nucleotides at a given position in the nucleic acid sequence. In those cases the ambiguities are denoted by an extended alphabet as follows:

These are the official IUPAC-IUB single-letter base codes

Code	Base Description	·
G	Guanine	
Α	Adenine	
T	Thymine	
C	Cytosine	·
R	Purine	(A or G)
Y	Pyrimidine	(C or T or U)
M	Amino	(A or C)
K	Ketone	(G or T)
S	Strong interaction	(C or G)
W	Weak interaction	(A or T)
H	Not-G	(A or C or T)
В	Not-A	(C or G or T)
<b>v</b> ,	Not-T (not-U)	(A or C or G)
D .	Not-C	(A or G or T)
N	Any	(A or C or G or T)

The amino acid translations of this invention account for the ambiguity in the nucleic acid sequence by translating the ambiguous codon as the letter "X". In all cases,

WO 98/18323 PCT/US97/19575

- 39 -

the permissible amino acid residues at a position are clear from an examination of the nucleic acid sequence based on the standard genetic code.

## V. Production of Fragments and Analogs of H. pylori Nucleic Acids and Polypeptides

Based on the discovery of the *H. pylori* gene products of the invention provided in the Sequence Lsiting, one skilled in the art can alter the disclosed structure (of *H. pylori* genes), e.g., by producing fragments or analogs, and test the newly produced structures for activity. Examples of techniques known to those skilled in the relevant art which allow the production and testing of fragments and analogs are discussed below. These, or analogous methods can be used to make and screen libraries of polypeptides, e.g., libraries of random peptides or libraries of fragments or analogs of cellular proteins for the ability to bind *H. pylori* polypeptides. Such screens are useful for the identification of inhibitors of *H. pylori*.

## 15 Generation of Fragments

5

10

20

25

30

35

Fragments of a protein can be produced in several ways, e.g., recombinantly, by proteolytic digestion, or by chemical synthesis. Internal or terminal fragments of a polypeptide can be generated by removing one or more nucleotides from one end (for a terminal fragment) or both ends (for an internal fragment) of a nucleic acid which encodes the polypeptide. Expression of the mutagenized DNA produces polypeptide fragments. Digestion with "end-nibbling" endonucleases can thus generate DNA's which encode an array of fragments. DNA's which encode fragments of a protein can also be generated by random shearing, restriction digestion or a combination of the above-discussed methods.

Fragments can also be chemically synthesized using techniques known in the art such as conventional Merrifield solid phase f-Moc or t-Boc chemistry. For example, peptides of the present invention may be arbitrarily divided into fragments of desired length with no overlap of the fragments, or divided into overlapping fragments of a desired length.

Alteration of Nucleic Acids and Polypeptides: Random Methods

Amino acid sequence variants of a protein can be prepared by random mutagenesis of DNA which encodes a protein or a particular domain or region of a protein. Useful methods include PCR mutagenesis and saturation mutagenesis. A library of random amino acid sequence variants can also be generated by the synthesis of a set of degenerate oligonucleotide sequences. (Methods for screening proteins in a library of variants are elsewhere herein).

# (A) PCR Mutagenesis

In PCR mutagenesis, reduced Taq polymerase fidelity is used to introduce random mutations into a cloned fragment of DNA (Leung et al., 1989, *Technique* 1:11-15). The DNA region to be mutagenized is amplified using the polymerase chain reaction (PCR) under conditions that reduce the fidelity of DNA synthesis by Taq DNA polymerase, e.g., by using a dGTP/dATP ratio of five and adding Mn<sup>2+</sup> to the PCR reaction. The pool of amplified DNA fragments are inserted into appropriate cloning vectors to provide random mutant libraries.

10

15

20

25

30

5

## (B) Saturation Mutagenesis

Saturation mutagenesis allows for the rapid introduction of a large number of single base substitutions into cloned DNA fragments (Mayers et al., 1985, Science 229:242). This technique includes generation of mutations, e.g., by chemical treatment or irradiation of single-stranded DNA in vitro. and synthesis of a complimentary DNA strand. The mutation frequency can be modulated by modulating the severity of the treatment, and essentially all possible base substitutions can be obtained. Because this procedure does not involve a genetic selection for mutant fragments both neutral substitutions, as well as those that alter function, are obtained. The distribution of point mutations is not biased toward conserved sequence elements.

# (C) Degenerate Oligonucleotides

A library of homologs can also be generated from a set of degenerate oligonucleotide sequences. Chemical synthesis of a degenerate sequences can be carried out in an automatic DNA synthesizer, and the synthetic genes then ligated into an appropriate expression vector. The synthesis of degenerate oligonucleotides is known in the art (see for example, Narang, SA (1983) *Tetrahedron* 39:3; Itakura et al. (1981) *Recombinant DNA*, *Proc* 3rd Cleveland Sympos. Macromolecules, ed. AG Walton, Amsterdam: Elsevier pp273-289; Itakura et al. (1984) Annu. Rev. Biochem. 53:323; Itakura et al. (1984) Science 198:1056; Ike et al. (1983) Nucleic Acid Res. 11:477. Such techniques have been employed in the directed evolution of other proteins (see, for example, Scott et al. (1990) Science 249:386-390; Roberts et al. (1992) PNAS 89:2429-2433; Devlin et al. (1990) Science 249: 404-406; Cwirla et al. (1990) PNAS 87: 6378-6382; as well as U.S. Patents Nos. 5,223,409, 5,198,346, and 5,096,815).

WO 98/18323 PCT/US97/19575

- 41 -

# Alteration of Nucleic Acids and Polypeptides: Methods for Directed Mutagenesis

Non-random or directed, mutagenesis techniques can be used to provide specific sequences or mutations in specific regions. These techniques can be used to create variants which include, e.g., deletions, insertions, or substitutions, of residues of the known amino acid sequence of a protein. The sites for mutation can be modified individually or in series, e.g., by (1) substituting first with conserved amino acids and then with more radical choices depending upon results achieved, (2) deleting the target residue, or (3) inserting residues of the same or a different class adjacent to the located site, or combinations of options 1-3.

10

15

20

25

30

35

## (A) Alanine Scanning Mutagenesis

Alanine scanning mutagenesis is a useful method for identification of certain residues or regions of the desired protein that are preferred locations or domains for mutagenesis, Cunningham and Wells (*Science* 244:1081-1085, 1989). In alanine scanning, a residue or group of target residues are identified (e.g., charged residues such as Arg, Asp, His, Lys, and Glu) and replaced by a neutral or negatively charged amino acid (most preferably alanine or polyalanine). Replacement of an amino acid can affect the interaction of the amino acids with the surrounding aqueous environment in or outside the cell. Those domains demonstrating functional sensitivity to the substitutions are then refined by introducing further or other variants at or for the sites of substitution. Thus, while the site for introducing an amino acid sequence variation is predetermined, the nature of the mutation per se need not be predetermined. For example, to optimize the performance of a mutation at a given site, alanine scanning or random mutagenesis may be conducted at the target codon or region and the expressed desired protein subunit variants are screened for the optimal combination of desired activity.

#### (B) Oligonucleotide-Mediated Mutagenesis

Oligonucleotide-mediated mutagenesis is a useful method for preparing substitution, deletion, and insertion variants of DNA, see, e.g., Adelman et al., (DNA 2:183, 1983). Briefly, the desired DNA is altered by hybridizing an oligonucleotide encoding a mutation to a DNA template, where the template is the single-stranded form of a plasmid or bacteriophage containing the unaltered or native DNA sequence of the desired protein. After hybridization, a DNA polymerase is used to synthesize an entire second complementary strand of the template that will thus incorporate the oligonucleotide primer, and will code for the selected alteration in the desired protein DNA. Generally, oligonucleotides of at least 25 nucleotides in length are used. An optimal oligonucleotide will have 12 to 15 nucleotides that are completely

10

15

20

25

30

35

complementary to the template on either side of the nucleotide(s) coding for the mutation. This ensures that the oligonucleotide will hybridize properly to the single-stranded DNA template molecule. The oligonucleotides are readily synthesized using techniques known in the art such as that described by Crea et al. (*Proc. Natl. Acad. Sci.* USA, 75: 5765[1978]).

#### (C) Cassette Mutagenesis

Another method for preparing variants, cassette mutagenesis, is based on the technique described by Wells et al. (Gene, 34:315[1985]). The starting material is a plasmid (or other vector) which includes the protein subunit DNA to be mutated. The codon(s) in the protein subunit DNA to be mutated are identified. There must be a unique restriction endonuclease site on each side of the identified mutation site(s). If no such restriction sites exist, they may be generated using the above-described oligonucleotide-mediated mutagenesis method to introduce them at appropriate locations in the desired protein subunit DNA. After the restriction sites have been introduced into the plasmid, the plasmid is cut at these sites to linearize it. A double-stranded oligonucleotide encoding the sequence of the DNA between the restriction sites but containing the desired mutation(s) is synthesized using standard procedures. The two strands are synthesized separately and then hybridized together using standard techniques. This double-stranded oligonucleotide is referred to as the cassette. This cassette is designed to have 3' and 5' ends that are comparable with the ends of the linearized plasmid, such that it can be directly ligated to the plasmid. This plasmid now contains the mutated desired protein subunit DNA sequence.

#### (D) Combinatorial Mutagenesis

Combinatorial mutagenesis can also be used to generate mutants (Ladner et al., WO 88/06630). In this method, the amino acid sequences for a group of homologs or other related proteins are aligned, preferably to promote the highest homology possible. All of the amino acids which appear at a given position of the aligned sequences can be selected to create a degenerate set of combinatorial sequences. The variegated library of variants is generated by combinatorial mutagenesis at the nucleic acid level, and is encoded by a variegated gene library. For example, a mixture of synthetic oligonucleotides can be enzymatically ligated into gene sequences such that the degenerate set of potential sequences are expressible as individual peptides, or alternatively, as a set of larger fusion proteins containing the set of degenerate sequences.

10

15

20

25

30

35

## Other Modifications of H. pylori Nucleic Acids and Polypeptides

It is possible to modify the structure of an *H. pylori* polypeptide for such purposes as increasing solubility, enhancing stability (e.g., shelf life *ex vivo* and resistance to proteolytic degradation *in vivo*). A modified *H. pylori* protein or peptide can be produced in which the amino acid sequence has been altered, such as by amino acid substitution, deletion, or addition as described herein.

An *H. pylori* peptide can also be modified by substitution of cysteine residues preferably with alanine, serine, threonine, leucine or glutamic acid residues to minimize dimerization via disulfide linkages. In addition, amino acid side chains of fragments of the protein of the invention can be chemically modified. Another modification is cyclization of the peptide.

In order to enhance stability and/or reactivity, an *H. pylori* polypeptide can be modified to incorporate one or more polymorphisms in the amino acid sequence of the protein resulting from any natural allelic variation. Additionally, D-amino acids, non-natural amino acids, or non-amino acid analogs can be substituted or added to produce a modified protein within the scope of this invention. Furthermore, an *H. pylori* polypeptide can be modified using polyethylene glycol (PEG) according to the method of A. Sehon and co-workers (Wie et al., supra) to produce a protein conjugated with PEG. In addition, PEG can be added during chemical synthesis of the protein. Other modifications of *H. pylori* proteins include reduction/alkylation (Tarr, *Methods of Protein Microcharacterization*, J. E. Silver ed., Humana Press, Clifton NJ 155-194 (1986)); acylation (Tarr, supra); chemical coupling to an appropriate carrier (Mishell and Shiigi, eds, *Selected Methods in Cellular Immunology*, WH Freeman, San Francisco, CA (1980), U.S. Patent 4,939,239; or mild formalin treatment (Marsh, (1971) *Int. Arch. of Allergy and Appl. Immunol.*, 41: 199 - 215).

To facilitate purification and potentially increase solubility of an *H. pylori* protein or peptide, it is possible to add an amino acid fusion moiety to the peptide backbone. For example, hexa-histidine can be added to the protein for purification by immobilized metal ion affinity chromatography (Hochuli, E. et al., (1988) *Bio/Technology*, 6: 1321 - 1325). In addition, to facilitate isolation of peptides free of irrelevant sequences, specific endoprotease cleavage sites can be introduced between the sequences of the fusion moiety and the peptide.

To potentially aid proper antigen processing of epitopes within an *H. pylori* polypeptide, canonical protease sensitive sites can be engineered between regions, each comprising at least one epitope via recombinant or synthetic methods. For example, charged amino acid pairs, such as KK or RR, can be introduced between regions within a protein or fragment during recombinant construction thereof. The resulting peptide

can be rendered sensitive to cleavage by cathepsin and/or other trypsin-like enzymes which would generate portions of the protein containing one or more epitopes. In addition, such charged amino acid residues can result in an increase in the solubility of the peptide.

5

10

15

20

25

30

35

# Primary Methods for Screening Polypeptides and Analogs

Various techniques are known in the art for screening generated mutant gene products. Techniques for screening large gene libraries often include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the genes under conditions in which detection of a desired activity, e.g., in this case, binding to *H. pylori* polypeptide or an interacting protein, facilitates relatively easy isolation of the vector encoding the gene whose product was detected. Each of the techniques described below is amenable to high through-put analysis for screening large numbers of sequences created, e.g., by random mutagenesis techniques.

## (A) Two Hybrid Systems

Two hybrid assays such as the system described above (as with the other screening methods described herein), can be used to identify polypeptides, e.g., fragments or analogs of a naturally-occurring *H. pylori* polypeptide, e.g., of cellular proteins, or of randomly generated polypeptides which bind to an *H. pylori* protein. (The *H. pylori* domain is used as the bait protein and the library of variants are expressed as fish fusion proteins.) In an analogous fashion, a two hybrid assay (as with the other screening methods described herein), can be used to find polypeptides which bind a *H. pylori* polypeptide.

## (B) Display Libraries

In one approach to screening assays, the candidate peptides are displayed on the surface of a cell or viral particle, and the ability of particular cells or viral particles to bind an appropriate receptor protein via the displayed product is detected in a "panning assay". For example, the gene library can be cloned into the gene for a surface membrane protein of a bacterial cell, and the resulting fusion protein detected by panning (Ladner et al., WO 88/06630; Fuchs et al. (1991) *Bio/Technology* 9:1370-1371; and Goward et al. (1992) *TIBS* 18:136-140). In a similar fashion, a detectably labeled ligand can be used to score for potentially functional peptide homologs. Fluorescently labeled ligands, e.g., receptors, can be used to detect homologs which retain ligand-binding activity. The use of fluorescently labeled ligands, allows cells to be visually

15

20

25

30

35

inspected and separated under a fluorescence microscope, or, where the morphology of the cell permits, to be separated by a fluorescence-activated cell sorter.

A gene library can be expressed as a fusion protein on the surface of a viral particle. For instance, in the filamentous phage system, foreign peptide sequences can be expressed on the surface of infectious phage, thereby conferring two significant benefits. First, since these phage can be applied to affinity matrices at concentrations well over 10<sup>13</sup> phage per milliliter, a large number of phage can be screened at one time. Second, since each infectious phage displays a gene product on its surface, if a particular phage is recovered from an affinity matrix in low yield, the phage can be amplified by another round of infection. The group of almost identical E. coli filamentous phages M13, fd., and fl are most often used in phage display libraries. Either of the phage gIII or gVIII coat proteins can be used to generate fusion proteins without disrupting the ultimate packaging of the viral particle. Foreign epitopes can be expressed at the NH2terminal end of pIII and phage bearing such epitopes recovered from a large excess of phage lacking this epitope (Ladner et al. PCT publication WO 90/02909; Garrard et al., PCT publication WO 92/09690; Marks et al. (1992) J. Biol. Chem. 267:16007-16010; Griffiths et al. (1993) EMBO J 12:725-734; Clackson et al. (1991) Nature 352:624-628; and Barbas et al. (1992) PNAS 89:4457-4461).

A common approach uses the maltose receptor of E. coli (the outer membrane protein, LamB) as a peptide fusion partner (Charbit et al. (1986) EMBO 5, 3029-3037). Oligonucleotides have been inserted into plasmids encoding the LamB gene to produce peptides fused into one of the extracellular loops of the protein. These peptides are available for binding to ligands, e.g., to antibodies, and can elicit an immune response when the cells are administered to animals. Other cell surface proteins, e.g., OmpA (Schorr et al. (1991) Vaccines 91, pp. 387-392), PhoE (Agterberg, et al. (1990) Gene 88, 37-45), and PAL (Fuchs et al. (1991) Bio/Tech 9, 1369-1372), as well as large bacterial surface structures have served as vehicles for peptide display. Peptides can be fused to pilin, a protein which polymerizes to form the pilus-a conduit for interbacterial exchange of genetic information (Thiry et al. (1989) Appl. Environ. Microbiol. 55, 984-993). Because of its role in interacting with other cells, the pilus provides a useful support for the presentation of peptides to the extracellular environment. Another large surface structure used for peptide display is the bacterial motive organ, the flagellum. Fusion of peptides to the subunit protein flagellin offers a dense array of many peptide copies on the host cells (Kuwajima et al. (1988) Bio/Tech. 6, 1080-1083). Surface proteins of other bacterial species have also served as peptide fusion partners. Examples include the Staphylococcus protein A and the outer membrane IgA protease of Neisseria (Hansson

10

15

20

25

30

35

et al. (1992) J. Bacteriol. 174, 4239-4245 and Klauser et al. (1990) EMBO J. 9, 1991-1999).

In the filamentous phage systems and the LamB system described above, the physical link between the peptide and its encoding DNA occurs by the containment of the DNA within a particle (cell or phage) that carries the peptide on its surface. Capturing the peptide captures the particle and the DNA within. An alternative scheme uses the DNA-binding protein LacI to form a link between peptide and DNA (Cull et al. (1992) PNAS USA 89:1865-1869). This system uses a plasmid containing the LacI gene with an oligonucleotide cloning site at its 3'-end. Under the controlled induction by arabinose, a LacI-peptide fusion protein is produced. This fusion retains the natural ability of LacI to bind to a short DNA sequence known as LacO operator (LacO). By installing two copies of LacO on the expression plasmid, the LacI-peptide fusion binds tightly to the plasmid that encoded it. Because the plasmids in each cell contain only a single oligonucleotide sequence and each cell expresses only a single peptide sequence, the peptides become specifically and stably associated with the DNA sequence that directed its synthesis. The cells of the library are gently lysed and the peptide-DNA complexes are exposed to a matrix of immobilized receptor to recover the complexes containing active peptides. The associated plasmid DNA is then reintroduced into cells for amplification and DNA sequencing to determine the identity of the peptide ligands. As a demonstration of the practical utility of the method, a large random library of dodecapeptides was made and selected on a monoclonal antibody raised against the opioid peptide dynorphin B. A cohort of peptides was recovered, all related by a consensus sequence corresponding to a six-residue portion of dynorphin B. (Cull et al. (1992) Proc. Natl. Acad. Sci. U.S.A. 89-1869)

This scheme, sometimes referred to as peptides-on-plasmids, differs in two important ways from the phage display methods. First, the peptides are attached to the C-terminus of the fusion protein, resulting in the display of the library members as peptides having free carboxy termini. Both of the filamentous phage coat proteins, pIII and pVIII, are anchored to the phage through their C-termini, and the guest peptides are placed into the outward-extending N-terminal domains. In some designs, the phage-displayed peptides are presented right at the amino terminus of the fusion protein. (Cwirla, et al. (1990) *Proc. Natl. Acad. Sci. U.S.A.* 87, 6378-6382) A second difference is the set of biological biases affecting the population of peptides actually present in the libraries. The LacI fusion molecules are confined to the cytoplasm of the host cells. The phage coat fusions are exposed briefly to the cytoplasm during translation but are rapidly secreted through the inner membrane into the periplasmic compartment, remaining anchored in the membrane by their C-terminal hydrophobic domains, with the

WO 98/18323

5

10

15

20

25

35

N-termini, containing the peptides, protruding into the periplasm while awaiting assembly into phage particles. The peptides in the LacI and phage libraries may differ significantly as a result of their exposure to different proteolytic activities. The phage coat proteins require transport across the inner membrane and signal peptidase processing as a prelude to incorporation into phage. Certain peptides exert a deleterious effect on these processes and are underrepresented in the libraries (Gallop et al. (1994) J. Med. Chem. 37(9):1233-1251). These particular biases are not a factor in the LacI display system.

The number of small peptides available in recombinant random libraries is enormous. Libraries of  $10^7$ - $10^9$  independent clones are routinely prepared. Libraries as large as  $10^{11}$  recombinants have been created, but this size approaches the practical limit for clone libraries. This limitation in library size occurs at the step of transforming the DNA containing randomized segments into the host bacterial cells. To circumvent this limitation, an *in vitro* system based on the display of nascent peptides in polysome complexes has recently been developed. This display library method has the potential of producing libraries 3-6 orders of magnitude larger than the currently available phage/phagemid or plasmid libraries. Furthermore, the construction of the libraries, expression of the peptides, and screening, is done in an entirely cell-free format.

In one application of this method (Gallop et al. (1994) J. Med. Chem. 37(9):1233-1251), a molecular DNA library encoding 10<sup>12</sup> decapeptides was constructed and the library expressed in an E. coli S30 in vitro coupled transcription/translation system. Conditions were chosen to stall the ribosomes on the mRNA, causing the accumulation of a substantial proportion of the RNA in polysomes and yielding complexes containing nascent peptides still linked to their encoding RNA. The polysomes are sufficiently robust to be affinity purified on immobilized receptors in much the same way as the more conventional recombinant peptide display libraries are screened. RNA from the bound complexes is recovered, converted to cDNA, and amplified by PCR to produce a template for the next round of synthesis and screening. The polysome display method can be coupled to the phage display system. Following several rounds of screening, cDNA from the enriched pool of polysomes was cloned into a phagemid vector. This vector serves as both a peptide expression vector, displaying peptides fused to the coat proteins, and as a DNA sequencing vector for peptide identification. By expressing the polysome-derived peptides on phage, one can either continue the affinity selection procedure in this format or assay the peptides on individual clones for binding activity in a phage ELISA, or for binding specificity in a completion phage ELISA (Barret, et al. (1992) Anal. Biochem 204,357-364). To

10

15

20

25

30

35

identify the sequences of the active peptides one sequences the DNA produced by the phagemid host.

# Secondary Screening of Polypeptides and Analogs

The high through-put assays described above can be followed by secondary screens in order to identify further biological activities which will, e.g., allow one skilled in the art to differentiate agonists from antagonists. The type of a secondary screen used will depend on the desired activity that needs to be tested. For example, an assay can be developed in which the ability to inhibit an interaction between a protein of interest and its respective ligand can be used to identify antagonists from a group of peptide fragments isolated though one of the primary screens described above.

Therefore, methods for generating fragments and analogs and testing them for activity are known in the art. Once the core sequence of interest is identified, it is routine for one skilled in the art to obtain analogs and fragments.

# Peptide Mimetics of H. pylori Polypeptides

The invention also provides for reduction of the protein binding domains of the subject *H. pylori* polypeptides to generate mimetics, e.g. peptide or non-peptide agents. The peptide mimetics are able to disrupt binding of a polypeptide to its counter ligand, e.g., in the case of an *H. pylori* polypeptide binding to a naturally occurring ligand. The critical residues of a subject *H. pylori* polypeptide which are involved in molecular recognition of a polypeptide can be determined and used to generate *H. pylori*-derived peptidomimetics which competitively or noncompetitively inhibit binding of the *H. pylori* polypeptide with an interacting polypeptide (see, for example, European patent applications EP-412,762A and EP-B31,080A).

For example, scanning mutagenesis can be used to map the amino acid residues of a particular *H. pylori* polypeptide involved in binding an interacting polypeptide, peptidomimetic compounds (e.g. diazepine or isoquinoline derivatives) can be generated which mimic those residues in binding to an interacting polypeptide, and which therefore can inhibit binding of an *H. pylori* polypeptide to an interacting polypeptide and thereby interfere with the function of *H. pylori* polypeptide. For instance, non-hydrolyzable peptide analogs of such residues can be generated using benzodiazepine (e.g., see Freidinger et al. in *Peptides: Chemistry and Biology*, G.R. Marshall ed., ESCOM Publisher: Leiden, Netherlands, 1988), azepine (e.g., see Huffman et al. in *Peptides: Chemistry and Biology*, G.R. Marshall ed., ESCOM Publisher: Leiden, Netherlands, 1988), substituted gama lactam rings (Garvey et al. in *Peptides: Chemistry and Biology*, G.R. Marshall ed., ESCOM Publisher: Leiden, Netherlands, 1988), keto-

10

15

20

25

30

35

methylene pseudopeptides (Ewenson et al. (1986) *J Med Chem* 29:295; and Ewenson et al. in *Peptides: Structure and Function* (Proceedings of the 9th American Peptide Symposium) Pierce Chemical Co. Rockland, IL, 1985), β-turn dipeptide cores (Nagai et al. (1985) *Tetrahedron Lett* 26:647; and Sato et al. (1986) *J Chem Soc Perkin Trans* 1:1231), and β-aminoalcohols (Gordon et al. (1985) *Biochem Biophys Res Commun* 134:71).

# VI. Vaccine Formulations for H. pylori Nucleic Acids and Polypeptides

This invention also features vaccine compositions or formulations (used interchangeably herein) for protection against infection by H. pylori or for treatment of H. pylori infection. As used herein, the term "treatment of H. pylori infection" refers to therapeutic treatment of an existing or established H. pylori infection. The terms "protection against H. pylori infection" or "prophylactic treatment" refer to the use of H. pylori vaccine formulation for reducing the risk of or preventing an infection in a subject at risk for H. pylori infection. In one embodiment, the vaccine compositions contain one or more immunogenic components, such as a surface protein, from H. pylori, or portion thereof, and a pharmaceutically acceptable carrier. For example, in one embodiment, the vaccine formulations of the invention contain at least one or combination of H. pylori polypeptides or fragments thereof, from same or different H. pylori antigens. Nucleic acids and H. pylori polypeptides for use in the vaccine formulations of the invention include the nucleic acids and polypeptides set forth in the Sequence Listing, preferably those H. pylori nucleic acids that encode surface proteins and surface proteins or fragments thereof. For example, a preferred nucleic acid and H. pylori polypeptide for use in a vaccine composition of the invention is selected from the group of nucleic acids which encode cell envelope proteins and H. pylori cell envelope proteins as set forth in Table 1. However, any nucleic acid encoding an immunogenic H. pylori protein and H. pylori polypetide, or portion thereof, can be used in the present invention. These vaccines have therapeutic and/or prophylactic utilities.

One aspect of the invention provides a vaccine composition for protection against infection by *H. pylori* which contains at least one immunogenic fragment of an *H. pylori* protein and a pharmaceutically acceptable carrier. Preferred fragments include peptides of at least about 10 amino acid residues in length, preferably about 10-20 amino acid residues in length, and more preferably about 12-16 amino acid residues in length.

Immunogenic components of the invention can be obtained, for example, by screening polypeptides recombinantly produced from the corresponding fragment of the nucleic acid encoding the full-length *H. pylori* protein. In addition, fragments can be

10

15

20

25

30

35

chemically synthesized using techniques known in the art such as conventional Merrifield solid phase f-Moc or t-Boc chemistry.

In one embodiment, immunogenic components are identified by the ability of the peptide to stimulate T cells. Peptides which stimulate T cells, as determined by, for example, T cell proliferation or cytokine secretion are defined herein as comprising at least one T cell epitope. T cell epitopes are believed to be involved in initiation and perpetuation of the immune response to the protein allergen which is responsible for the clinical symptoms of allergy. These T cell epitopes are thought to trigger early events at the level of the T helper cell by binding to an appropriate HLA molecule on the surface of an antigen presenting cell, thereby stimulating the T cell subpopulation with the relevant T cell receptor for the epitope. These events lead to T cell proliferation, lymphokine secretion, local inflammatory reactions, recruitment of additional immune cells to the site of antigen/T cell interaction, and activation of the B cell cascade, leading to the production of antibodies. A T cell epitope is the basic element, or smallest unit of recognition by a T cell receptor, where the epitope comprises amino acids essential to receptor recognition (e.g., approximately 6 or 7 amino acid residues). Amino acid sequences which mimic those of the T cell epitopes are within the scope of this invention.

In another embodiment, immunogenic components of the invention are identified through genomic vaccination. The basic protocol is based on the idea that expression libraries consisting of all or parts of a pathogen genome, e.g., an *H. pylori* genome, can confer protection when used to genetically immunize a host. This expression library immunization (ELI) is analogous to expression cloning and involves reducing a genomic expression library of a pathogen, e.g., *H. pylori*, into plasmids that can act as genetic vaccines. The plasmids can also be designed to encode genetic adjuvants which can dramatically stimulate the humoral response. These genetic adjuvants can be introduced at remote sites and act as well extracelluraly as intracellularly.

This is a new approach to vaccine production that has many of the advantages of live/attenuated pathogens but no risk of infection. An expression library of pathogen DNA is used to immunize a host thereby producing the effects of antigen presentation of a live vaccine without the risk. For example, in the present invention, random fragments from the *H. pylori* genome or from cosmid or plasmid clones, as well as PCR products from genes identified by genomic sequencing, can be used to immunize a host. The feasibility of this approach has been demonstrated with *Mycoplasma pulmonis* (Barry et al., *Nature* 377:632-635, 1995), where even partial expression libraries of *Mycoplasma pulmonis*, a natural pathogen in rodents, provided protection against challenge from the pathogen.

10

15

25

30

35

ELI is a technique that allows for production of a non-infectious multipartite vaccine, even when little is known about pathogen's biology, because ELI uses the immune system to screen candidate genes. Once isolated, these genes can be used as genetic vaccines or for development of recombinant protein vaccines. Thus, ELI allows for production of vaccines in a systematic, largely mechanized fashion.

Screening immunogenic components can be accomplished using one or more of several different assays. For example, *in vitro*, peptide T cell stimulatory activity is assayed by contacting a peptide known or suspected of being immunogenic with an antigen presenting cell which presents appropriate MHC molecules in a T cell culture. Presentation of an immunogenic *H. pylori* peptide in association with appropriate MHC molecules to T cells in conjunction with the necessary costimulation has the effect of transmitting a signal to the T cell that induces the production of increased levels of cytokines, particularly of interleukin-2 and interleukin-4. The culture supernatant can be obtained and assayed for interleukin-2 or other known cytokines. For example, any one of several conventional assays for interleukin-2 can be employed, such as the assay described in *Proc. Natl. Acad. Sci USA*, 86: 1333 (1989) the pertinent portions of which are incorporated herein by reference. A kit for an assay for the production of interferon is also available from Genzyme Corporation (Cambridge, MA).

Alternatively, a common assay for T cell proliferation entails measuring tritiated thymidine incorporation. The proliferation of T cells can be measured *in vitro* by determining the amount of <sup>3</sup>H-labeled thymidine incorporated into the replicating DNA of cultured cells. Therefore, the rate of DNA synthesis and, in turn, the rate of cell division can be quantified.

Vaccine compositions or formulations of the invention containing one or more immunogenic components (e.g., *H. pylori* polypeptide or fragment thereof or nucleic acid encoding an *H. pylori* polypeptide or fragment thereof) preferably include a pharmaceutically acceptable carrier. The term "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. Suitable pharmaceutically acceptable carriers include, for example, one or more of water, saline, phosphate buffered saline, dextrose, glycerol, ethanol and the like, as well as combinations thereof. Pharmaceutically acceptable carriers may further comprise minor amounts of auxiliary substances such as wetting or emulsifying agents, preservatives or buffers, which enhance the shelf life or effectiveness of the *H. pylori* nucleic acid or polypeptide. For vaccine formulations of the invention containing *H. pylori* polypeptides, the polypeptide is preferably coadministered with a suitable adjuvant and/or a delivery system described herein.

10

15

35

It will be apparent to those of skill in the art that the therapeutically effective amount of DNA or protein of this invention will depend, *inter alia*, upon the administration schedule, the unit dose of an *H. pylori* nucleic acid or polypeptide administered, whether the protein or nucleic acid is administered in combination with other therapeutic agents, the immune status and health of the patient, and the therapeutic activity of the particular protein or nucleic acid.

Vaccine formulations are conventionally administered parenterally, e.g., by injection, either subcutaneously or intramuscularly. Methods for intramuscular immunization are described by Wolff et al. (1990) Science 247: 1465-1468 and by Sedegah et al. (1994) Immunology 91: 9866-9870. Other modes of administration include oral and pulmonary formulations, suppositories, and transdermal applications. Oral immunization is preferred over parenteral methods for inducing protection against infection by H. pylori. Czinn et. al. (1993) Vaccine 11: 637-642. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, and the like.

In one embodiment, the vaccine formulation includes, as a pharmaceutically acceptable carrier, an adjuvant. Examples of the suitable adjuvants for use in the vaccine formulations of the invention include, but are not limited, to aluminum hydroxide; N-acetyl-muramyl--L-threonyl-D-isoglutamine (thr-MDP); N-acetyl-nor-20 muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP); Nacetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3hydroxyphos-phoryloxy)-ethylamine (CGP 19835A, referred to a MTP-PE); RIBI, which contains three components from bacteria; monophosphoryl lipid A; trehalose dimycoloate; cell wall skeleton (MPL + TDM + CWS) in a 2% squalene/Tween 80 25 emulsion; and cholera toxin. Others which may be used are non-toxic derivatives of cholera toxin, including its B subunit, and/or conjugates or genetically engineered fusions of the H. pylori polypeptide with cholera toxin or its B subunit, procholeragenoid, fungal polysaccharides, including schizophyllan, muramyl dipeptide, muramyl dipeptide derivatives, phorbol esters, labile toxin of E. coli, non-H. pylori 30 bacterial lysates, block polymers or saponins.

In another embodiment, the vaccine formulation includes, as a pharmaceutically acceptable carrier, a delivery system. Suitable delivery systems for use in the vaccine formulations of the invention include biodegradable microcapsules or immunostimulating complexes (ISCOMs), cochleates, or liposomes, genetically engineered attenuated live vectors such as viruses or bacteria, and recombinant (chimeric) virus-like

10

15

20

25

30

35

particles, e.g., bluetongue. In another embodiment of the invention, the vaccine formulation includes both a delivery system and an adjuvant.

Delivery systems in humans may include enteric release capsules protecting the antigen from the acidic environment of the stomach, and including *H. pylori* polypeptide in an insoluble form as fusion proteins. Suitable carriers for the vaccines of the invention are enteric coated capsules and polylactide-glycolide microspheres. Suitable diluents are 0.2 N NaHCO3 and/or saline.

Vaccines of the invention can be administered as a primary prophylactic agent in adults or in children, as a secondary prevention, after successful eradication of H. pylori in an infected host, or as a therapeutic agent in the aim to induce an immune response in a susceptible host to prevent infection by H. pylori. The vaccines of the invention are administered in amounts readily determined by persons of ordinary skill in the art. Thus, for adults a suitable dosage will be in the range of 10  $\mu$ g to 10 g, preferably 10  $\mu$ g to 100 mg, for example 50  $\mu$ g to 50 mg. A suitable dosage for adults will also be in the range of 5  $\mu$ g to 500 mg. Similar dosage ranges will be applicable for children.

The amount of adjuvant employed will depend on the type of adjuvant used. For example, when the mucosal adjuvant is cholera toxin, it is suitably used in an amount of 5  $\mu$ g to 50  $\mu$ g, for example 10  $\mu$ g to 35  $\mu$ g. When used in the form of microcapsules, the amount used will depend on the amount employed in the matrix of the microcapsule to achieve the desired dosage. The determination of this amount is within the skill of a person of ordinary skill in the art.

Those skilled in the art will recognize that the optimal dose may be more or less depending upon the patient's body weight, disease, the route of administration, and other factors. Those skilled in the art will also recognize that appropriate dosage levels can be obtained based on results with known oral vaccines such as, for example, a vaccine based on an *E. coli* lysate (6 mg dose daily up to total of 540 mg) and with an enterotoxigenic *E. coli* purified antigen (4 doses of 1 mg) (Schulman et al., *J. Urol.* 150:917-921 (1993)); Boedecker et al., *American Gastroenterological Assoc.* 999:A-222 (1993)). The number of doses will depend upon the disease, the formulation, and efficacy data from clinical trials. Without intending any limitation as to the course of treatment, the treatment can be administered over 3 to 8 doses for a primary immunization schedule over 1 month (Boedeker, *American Gastroenterological Assoc.* 888:A-222 (1993)).

In a preferred embodiment, a vaccine composition of the invention can be based on a killed whole *E. coli* preparation with an immunogenic fragment of an *H. pylori* protein of the invention expressed on its surface or it can be based on an *E. coli* lysate, wherein the killed *E. coli* acts as a carrier or an adjuvant.

It will be apparent to those skilled in the art that some of the vaccine compositions of the invention are useful only for preventing *H. pylori* infection, some are useful only for treating *H. pylori* infection, and some are useful for both preventing and treating *H. pylori* infection. In a preferred embodiment, the vaccine composition of the invention provides protection against *H. pylori* infection by stimulating humoral and/or cell-mediated immunity against *H. pylori*. It should be understood that amelioration of any of the symptoms of *H. pylori* infection is a desirable clinical goal, including a lessening of the dosage of medication used to treat *H. pylori*-caused disease, or an increase in the production of antibodies in the serum or mucous of patients.

10

15

20

25

30

35

5

# VII. Antibodies Reactive With H. pylori Polypeptides

The invention also includes antibodies specifically reactive with the subject *H. pylori* polypeptide. Anti-protein/anti-peptide antisera or monoclonal antibodies can be made by standard protocols (See, for example, *Antibodies: A Laboratory Manual* ed. by Harlow and Lane (Cold Spring Harbor Press: 1988)). A mammal such as a mouse, a hamster or rabbit can be immunized with an immunogenic form of the peptide. Techniques for conferring immunogenicity on a protein or peptide include conjugation to carriers or other techniques well known in the art. An immunogenic portion of the subject *H. pylori* polypeptide can be administered in the presence of adjuvant. The progress of immunization can be monitored by detection of antibody titers in plasma or serum. Standard ELISA or other immunoassays can be used with the immunogen as antigen to assess the levels of antibodies.

In a preferred embodiment, the subject antibodies are immunospecific for antigenic determinants of the *H. pylori* polypeptides of the invention, e.g. antigenic determinants of a polypeptide of the invention contained in the Sequence Listing, or a closely related human or non-human mammalian homolog (e.g., 90% homologous, more preferably at least 95% homologous). In yet a further preferred embodiment of the invention, the anti-*H. pylori* antibodies do not substantially cross react (i.e., react specifically) with a protein which is for example, less than 80% percent homologous to a sequence of the invention contained in the Sequence Listing. By "not substantially cross react", it is meant that the antibody has a binding affinity for a non-homologous protein which is less than 10 percent, more preferably less than 5 percent, and even more preferably less than 1 percent, of the binding affinity for a protein of the invention contained in the Sequence Listing. In a most preferred embodiment, there is no crossreactivity between bacterial and mammalian antigens.

The term antibody as used herein is intended to include fragments thereof which are also specifically reactive with *H. pylori* polypeptides. Antibodies can be fragmented

10

15

20

25

30

35

using conventional techniques and the fragments screened for utility in the same manner as described above for whole antibodies. For example, F(ab')<sub>2</sub> fragments can be generated by treating antibody with pepsin. The resulting F(ab')<sub>2</sub> fragment can be treated to reduce disulfide bridges to produce Fab' fragments. The antibody of the invention is further intended to include bispecific and chimeric molecules having an anti-H. pylori portion.

Both monoclonal and polyclonal antibodies (Ab) directed against *H. pylori* polypeptides or *H. pylori* polypeptide variants, and antibody fragments such as Fab' and F(ab')2, can be used to block the action of *H. pylori* polypeptide and allow the study of the role of a particular *H. pylori* polypeptide of the invention in aberrant or unwanted intracellular signaling, as well as the normal cellular function of the *H. pylori* and by microinjection of anti-*H. pylori* polypeptide antibodies of the present invention.

Antibodies which specifically bind *H. pylori* epitopes can also be used in immunohistochemical staining of tissue samples in order to evaluate the abundance and pattern of expression of *H. pylori* antigens. Anti *H. pylori* polypeptide antibodies can be used diagnostically in immuno-precipitation and immuno-blotting to detect and evaluate *H. pylori* levels in tissue or bodily fluid as part of a clinical testing procedure. Likewise, the ability to monitor *H. pylori* polypeptide levels in an individual can allow determination of the efficacy of a given treatment regimen for an individual afflicted with such a disorder. The level of an *H. pylori* polypeptide can be measured in cells found in bodily fluid, such as in urine samples or can be measured in tissue, such as produced by gastric biopsy. Diagnostic assays using anti-*H. pylori* antibodies can include, for example, immunoassays designed to aid in early diagnosis of *H. pylori* infections. The present invention can also be used as a method of detecting antibodies contained in samples from individuals infected by this bacterium using specific *H. pylori* antigens.

Another application of anti-*H. pylori* polypeptide antibodies of the invention is in the immunological screening of cDNA libraries constructed in expression vectors such as  $\lambda gt11$ ,  $\lambda gt18-23$ ,  $\lambda ZAP$ , and  $\lambda ORF8$ . Messenger libraries of this type, having coding sequences inserted in the correct reading frame and orientation, can produce fusion proteins. For instance,  $\lambda gt11$  will produce fusion proteins whose amino termini consist of  $\beta$ -galactosidase amino acid sequences and whose carboxy termini consist of a foreign polypeptide. Antigenic epitopes of a subject *H. pylori* polypeptide can then be detected with antibodies, as, for example, reacting nitrocellulose filters lifted from infected plates with anti-*H. pylori* polypeptide antibodies. Phage, scored by this assay, can then be isolated from the infected plate. Thus, the presence of *H. pylori* gene

10

15

20

25

30

35

homologs can be detected and cloned from other species, and alternate isoforms (including splicing variants) can be detected and cloned.

# VIII. Kits Containing Nucleic Acids, Polypeptides or Antibodies of the Invention

The nucleic acid, polypeptides and antibodies of the invention can be combined with other reagents and articles to form kits. Kits for diagnostic purposes typically comprise the nucleic acid, polypeptides or antibodies in vials or other suitable vessels. Kits typically comprise other reagents for performing hybridization reactions, polymerase chain reactions (PCR), or for reconstitution of lyophilized components, such as aqueous media, salts, buffers, and the like. Kits may also comprise reagents for sample processing such as detergents, chaotropic salts and the like. Kits may also comprise immobilization means such as particles, supports, wells, dipsticks and the like. Kits may also comprise labeling means such as dyes, developing reagents, radioisotopes, fluorescent agents, luminescent or chemiluminescent agents, enzymes, intercalating agents and the like. With the nucleic acid and amino acid sequence information provided herein, individuals skilled in art can readily assemble kits to serve their particular purpose. Kits further can include instructions for use.

# IX. Drug Screening Assays Using H. pylori Polypeptides

By making available purified and recombinant *H. pylori* polypeptides, the present invention provides assays which can be used to screen for drugs which are either agonists or antagonists of the normal cellular function, in this case, of the subject *H. pylori* polypeptides, or of their role in intracellular signaling. Such inhibitors or potentiators may be useful as new therapeutic agents to combat *H. pylori* infections in humans. A variety of assay formats will suffice and, in light of the present inventions, will be comprehended by the skilled artisan.

In many drug screening programs which test libraries of compounds and natural extracts, high throughput assays are desirable in order to maximize the number of compounds surveyed in a given period of time. Assays which are performed in cell-free systems, such as may be derived with purified or semi-purified proteins, are often preferred as "primary" screens in that they can be generated to permit rapid development and relatively easy detection of an alteration in a molecular target which is mediated by a test compound. Moreover, the effects of cellular toxicity and/or bioavailability of the test compound can be generally ignored in the *in vitro* system, the assay instead being focused primarily on the effect of the drug on the molecular target as may be manifest in an alteration of binding affinity with other proteins or change in enzymatic properties of the molecular target. Accordingly, in an exemplary screening assay of the present

10

15

20

25

30

35

invention, the compound of interest is contacted with an isolated and purified *H. pylori* polypeptide.

Screening assays can be constructed *in vitro* with a purified *H. pylori* polypeptide or fragment thereof, such as an *H. pylori* polypeptide having enzymatic activity, such that the activity of the polypeptide produces a detectable reaction product. The efficacy of the compound can be assessed by generating dose response curves from data obtained using various concentrations of the test compound. Moreover, a control assay can also be performed to provide a baseline for comparison. Suitable products include those with distinctive absorption, fluorescence, or chemi-luminescence properties, for example, because detection may be easily automated. A variety of synthetic or naturally occurring compounds can be tested in the assay to identify those which inhibit or potentiate the activity of the *H. pylori* polypeptide. Some of these active compounds may directly, or with chemical alterations to promote membrane permeability or solubility, also inhibit or potentiate the same activity (e.g., enzymatic activity) in whole, live *H. pylori* cells.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references and published patent applications cited throughout this application are hereby incorporated by reference.

#### **EXEMPLIFICATION**

## I. Cloning and Sequencing of H. pylori DNA

H. pylori chromosomal DNA was isolated according to a basic DNA protocol outlined in Schleif R.F. and Wensink P.C., Practical Methods in Molecular Biology, p.98, Springer-Verlag, NY., 1981, with minor modifications. Briefly, cells were pelleted, resuspended in TE (10 mM Tris, 1 mM EDTA, pH 7.6) and GES lysis buffer (5.1 M guanidium thiocyanate, 0.1 M EDTA, pH 8.0, 0.5% N-laurylsarcosine) was added. Suspension was chilled and ammonium acetate (NH<sub>4</sub>Ac) was added to final concentration of 2.0 M. DNA was extracted, first with chloroform, then with phenol-chloroform, and reextracted with chloroform. DNA was precipitated with isopropanol, washed twice with 70% EtOH, dried and resuspended in TE.

Following isolation whole genomic *H. pylori* DNA was nebulized (Bodenteich et al., *Automated DNA Sequencing and Analysis* (J.C. Venter, ed.), Academic Press, 1994) to a median size of 2000 bp. After nebulization, the DNA was concentrated and separated on a standard 1% agarose gel. Several fractions, corresponding to

10

15

20

25

30

35

approximate sizes 900-1300 bp, 1300-1700 bp, 1700-2200 bp, 2200-2700 bp, were excised from the gel and purified by the GeneClean procedure (Bio101, Inc.).

The purified DNA fragments were then blunt-ended using T4 DNA polymerase. The healed DNA was then ligated to unique BstXI-linker adapters in 100-1000 fold molar excess. These linkers are complimentary to the BstXI-cut pMPX vectors, while the overhang is not self-complimentary. Therefore, the linkers will not concatemerize nor will the cut-vector religate itself easily. The linker-adopted inserts were separated from the unincorporated linkers on a 1% agarose gel and purified using GeneClean. The linker-adopted inserts were then ligated to each of the 20 pMPX vectors to construct a series of "shotgun" subclone libraries. The vectors contain an out-of-frame lacZ gene at the cloning site which becomes in-frame in the event that an adapter-dimer is cloned, allowing these to be avoided by their blue-color.

All subsequent steps were based on the multiplex DNA sequencing protocols outlined in Church G.M. and Kieffer-Higgins S., *Science* 240:185-188, 1988. Only major modifications to the protocols are highlighted. Briefly, each of the 20 vectors was then transformed into DH5α competent cells (Gibco/BRL, DH5α transformation protocol). The libraries were assessed by plating onto antibiotic plates containing ampicillin, methicillin and IPTG/Xgal. The plates were incubated overnight at 37°C. Successful transformants were then used for plating of clones and pooling into the multiplex pools. The clones were picked and pooled into 40 ml growth medium cultures. The cultures were grown overnight at 37°C. DNA was purified using the Qiagen Midi-prep kits and Tip-100 columns (Qiagen, Inc.). In this manner, 100 μg of DNA was obtained per pool. Fifteen 96-well plates of DNA were generated to obtain a 5-10 fold sequence redundancy assuming 250-300 base average read-lengths.

These purified DNA samples were then sequenced using the multiplex DNA sequencing based on chemical degradation methods (Church G.M. and Kieffer-Higgins S., Science 240:185-188, 1988) or by Sequithrem (Epicenter Technologies) dideoxy sequencing protocols. The sequencing reactions were electrophoresed and transferred onto nylon membranes by direct transfer electrophoresis from 40 cm gels (Richterich P. and Church G.M., Methods in Enzymology 218:187-222, 1993) or by electroblotting (Church, supra). 24 samples were run per gel. 45 successful membranes were produced by chemical sequencing and 8 were produced by dideoxy sequencing. The DNA was covalently bound to the membranes by exposure to ultraviolet light, and hybridized with labeled oligonucleotides complimentary to tag sequences on the vectors (Church, supra). The membranes were washed to rinse off non-specifically bound probe, and exposed to X-ray film to visualize individual sequence ladders. After autoradiography, the hybridized probe was removed by incubation at 65° C, and the hybridization cycle

15

20 .

25

35

repeated with another tag sequence until the membrane had been probed 38 times for chemical sequencing membranes and 10 times for the dideoxy sequencing membranes. Thus, each gel produced a large number of films, each containing new sequencing information. Whenever a new blot was processed, it was initially probed for an internal standard sequence added to each of the pools.

Digital images of the films were generated using a laser-scanning densitometer (Molecular Dynamics, Sunnyvale, CA). The digitized images were processed on computer workstations (VaxStation 4000's) using the program REPLICA™ (Church et al., Automated DNA Sequencing and Analysis (J.C. Venter, ed.), Academic Press, 1994). Image processing included lane straightening, contrast adjustment to smooth out intensity differences, and resolution enhancement by iterative gaussian deconvolution. The sequences were then automatically picked in REPLICATM and displayed for interactive proofreading before being stored in a project database. The proofreading was accomplished by a quick visual scan of the film image followed by mouse clicks on the bands of the displayed image to modify the base calls. Many of the sequence errors could be detected and corrected because multiple sequence reads covering the same portion of the genomic DNA provide adequate sequence redundancy for editing. Each sequence automatically received an identification number (corresponding to microtiter plate, probe information, and lane set number). This number serves as a permanent identifier of the sequence so it is always possible to identify the original of any particular sequence without recourse to a specialized database.

Routine assembly of *H. pylori* sequences was done using the program FALCON (Church, Church et al., *Automated DNA Sequenicng and Analysis* (J.C. Venter, ed.), Academic Press, 1994). This program has proven to be fast and reliable for most sequences. The assembled contigs were displayed using a modified version of GelAssemble, developed by the Genetics Computer Group (GCG) (Devereux et al., *Nucleic Acid Res.* 12:387-95, 1984) that interacts with REPLICA<sup>TM</sup>. This provided for an integrated editor that allows multiple sequence gel images to be instantaneously called up from the REPLICA<sup>TM</sup> database and displayed to allow rapid scanning of contigs and proofreading of gel traces where discrepancies occurred between different sequence reads in the assembly.

# II. Identification, cloning and expression of recombinant H. pylori DNA sequences

To facilitate the cloning, expression and purification of membrane and secreted proteins from *H. pylori* a powerful gene expression system, the pET System (Novagen), for cloning and expression of recombinant proteins in *E. coli*, was selected. Also, a DNA sequence encoding a peptide tag, the His-Tag, was fused to the 3' end of DNA

sequences of interest in order to facilitate purification of the recombinant protein products. The 3' end was selected for fusion in order to avoid alteration of any 5' terminal signal sequence. The exception to the above was ppiB, a gene cloned for use as a control in the expression studies. In this study, the sequence for *H. pylori* ppiB contains a DNA sequence encoding a His-Tag fused to the 5' end of the full length gene, because the protein product of this gene does not contain a signal sequence and is expressed as a cytosolic protein.

PCR Amplification and cloning of DNA sequences containing ORF's for membrane and secreted proteins from the J99 Strain of Helicobacter pylori.

Sequences chosen (from the list of the DNA sequences of the invention) for cloning from the J99 strain of H. pylori were prepared for amplification cloning by polymerase chain reaction (PCR). Synthetic oligonucleotide primers (Table 3) specific for the 5' and 3' ends of open reading frames (ORFs) were designed and purchased 15 (GibcoBRL Life Technologies, Gaithersburg, MD, USA). All forward primers (specific for the 5' end of the sequence) were designed to include an Ncol cloning site at the extreme 5' terminus, except for HpSeq. 4821082 where Ndel was used. These primers were designed to permit initiation of protein translation at a methionine residue followed by a valine residue and the coding sequence for the remainder of the native H. pylori DNA sequence. An exception is H. pylori sequence 4821082 where the initiator 20 methionine is immediately followed by the remainder of the native H. pylori DNA sequence. All reverse primers (specific for the 3' end of any H. pylori ORF) included a EcoRI site at the extreme 5' terminus to permit cloning of each H. pylori sequence into the reading frame of the pET-28b. The pET-28b vector provides sequence encoding an additional 20 carboxy-terminal amino acids (only 19 amino acids in HpSeq. 26380318 25 and HpSeq.14640637) including six histidine residues (at the extreme C-terminus), which comprise the His-Tag. An exception to the above, as noted earlier, is the vector construction for the ppiB gene. A synthetic oligonucleotide primer specific for the 5' end of ppiB gene encoded a BamHI site at its extreme 5' terminus and the primer for the 3' end of the ppiB gene encoded a XhoI site at its extreme 5' terminus. 30

<u>TABLE 3</u>
<u>Oligonucleotide primers used for PCR amplification of *H. pylori* DNA sequences</u>

Outer membrane Proteins	Forward primer 5' to 3'	Reverse Primer 5' to 3'		
Protein 16225006	5'-TATACCATGGTGGG CGCTAA-3' (SEQ ID NO:147)	5'- ATGAATTCGAGTAAC GATTTTTG-3' (SEQ ID NO:148)		
Protein 26054702	5'- TTAACCATGGTGAAA AGCGATA-3' (SEQ ID NO:149)	5'- TAGAATTCGCATAAC GATCAATC-3' (SEQ ID NO:150)		
Protein 7116626	5'- ATATCCATGGTGAGT TTGATGA-3' (SEQ ID NO:151)	5'- ATGAATTCAATTTT TATTTTGCCA-3' (SEQ ID NO:152)		
Protein 29479681	5'- AATTCCATGGTGGGG GCTATG-3' (SEQ ID NO:153)	5'- ATGAATTCTCGATAG CCAAAATC-3' (SEQ ID NO:154)		
Protein 14640637	5'- AATTCCATGGTGCAT AACTTCCATT-3' (SEQ ID NO:155)	5'- AAGAATTCTCTAGCA TCCAAATGGA-3' (SEQ ID NO:156)		
Periplasmic/ Secreted Proteins		·		
Protein 30100332	5'-ATTTCCATGGTCATG TCTCATATT-3' (SEQ ID NO:157)	5'- ATGAATTCCATCTTT TATTCCAC-3' (SEQ ID NO:158)		
Protein 4721061	5'-AACCATGGTGATTT TAAGCATTGAAAG-3' (SEQ ID NO:159)	5'- AAGAATTCCACTCA AAATTTTTTAACAG-3' (SEQ ID NO:160)		
Other Surface Proteins		·		
Protein 4821082	5'-GATCATCCATATGTT ATCTTCTAAT-3' (SEQ ID NO:161)	5'- TGAATTCAACCATTT TAACCCTG-3' (SEQ ID NO:162)		

Protein 978477	5'-TATACCATGGTGAA ATTTTTTCTTTTA-3' (SEQ ID NO:163)	5'- AGAATTCAATTGCG TCTTGTAAAAG-3' (SEQ ID NO:164)
Inner Membrane		
Protein		
Protein 26380318	5'-TATACCATGGTGAT	5'-ATGAATTCCCACTT
·	GGACAAACTC-3' (SEQ	GGGGCGATA-3' (SEQ
	ID NO:165)	ID NO:166)
Cytoplasmic Protein		
	<u> </u>	
ppi	5'-TTATGGATCCAAAC	5'-TATCTCGAGTTATA
	CAATTAAAACT-3' (SEQ	GAGAAGGGC-3' (SEQ
	ID NO:167)	ID NO:168)

Genomic DNA prepared from the J99 strain of *H. pylori* (ATCC #55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) was used as the source of template DNA for PCR amplification reactions

(Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). To amplify a DNA sequence containing an *H. pylori* ORF, genomic DNA (50 nanograms) was introduced into a reaction vial containing 2 mM MgCl<sub>2</sub>, 1 micromolar synthetic oligonucleotide primers (forward and reverse primers) complementary to and flanking a defined *H. pylori* ORF, 0.2 mM of each deoxynucleotide triphosphate; dATP, dGTP, dCTP, dTTP and 2.5 units of heat stable DNA polymerase (Amplitaq, Roche Molecular Systems, Inc., Branchburg, NJ, USA) in a final volume of 100 microliters. The following thermal cycling conditions were used to obtain amplified DNA products for each ORF using a Perkin Elmer Cetus/ GeneAmp PCR System 9600 thermal cycler:

15

# Protein 26054702, Protein 7116626, Protein 29479681, Protein 30100332, and Protein 4821082;

Denaturation at 94°C for 2 min,

2 cycles at 94°C for 15 sec, 30°C for 15 sec and 72°C for 1.5 min

23 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min

Reactions were concluded at 72°C for 6 minutes.

# Protein 16225006;

Denaturation at 94°C for 2 min.

25 cycles at 95°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min Reaction was concluded at 72°C for 6 minutes.

## Protein 4721061;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 36°C for 15 sec and 72°C for 1.5 min 23 cycles at 94°C for 15 sec, 60°C for 15 sec and 72°C for 1.5 min Reactions were concluded at 72°C for 6 minutes.

#### Protein 26380318;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 38°C for 15 sec and 72°C for 1.5 min 23 cycles at 94°C for 15 sec, 62°C for 15 sec and 72°C for 1.5 min Reactions were concluded at 72°C for 6 minutes.

#### Protein 14640637;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 33°C for 15 sec and 72°C for 1.5 min 30 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min Reactions were concluded at 72°C for 6 minutes.

## Conditions for amplification of H. pylori ppiB;

Denaturation at 94°C for 2 min.

2 cycles at 94°C for 15 sec, 32°C for 15 sec and 72°C for 1.5 min

25 cycles at 94°C for 15 sec, 56°C for 15 sec and 72°C for 1.5 min

Reactions were concluded at 72°C for 6 minutes

Upon completion of thermal cycling reactions, each sample of amplified DNA was washed and purified using the Qiaquick Spin PCR purification kit (Qiagen, Gaithersburg, MD, USA). All amplified DNA samples were subjected to digestion with the restriction endonucleases, Ncol and EcoRI (New England BioLabs, Beverly, MA, USA), or in the case of HpSeq. 4821082 (SEQ ID NO: 1309), with Ndel and EcoRI (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). DNA samples were then subjected to electrophoresis on 1.0 % NuSeive (FMC BioProducts, Rockland, ME USA) agarose gels. DNA was visualized by exposure to ethidium bromide and long wave uv irradiation. DNA contained in slices

isolated from the agarose gel was purified using the Bio 101 GeneClean Kit protocol (Bio 101 Vista, CA, USA).

Cloning of H. pylori DNA sequences into the pET-28b prokaryotic expression vector.

The pET-28b vector was prepared for cloning by digestion with <u>Ncol</u> and <u>EcoRI</u>, or in the case of *H. pylori* protein 4821082 with <u>Ndel</u> and <u>EcoRI</u> (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). In the case of cloning ppiB, the pET-28a vector, which encodes a His-Tag that can be fused to the 5' end of an inserted gene, was used and the cloning site prepared for cloning with the ppiB gene by digestion with <u>BamHI</u> and <u>XhoI</u> restriction endonucleases.

Following digestion, DNA inserts were cloned (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994) into the previously digested pET-28b expression vector, except for the amplified insert for ppiB, which was cloned into the pET-28a expression vector. Products of the ligation reaction were then used to transform the BL21 strain of *E. coli* (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994) as described below.

# Transformation of competent bacteria with recombinant plasmids

Competent bacteria, *E coli* strain BL21 or *E. coli* strain BL21(DE3), were transformed with recombinant pET expression plasmids carrying the cloned *H. pylori* sequences according to standard methods (Current Protocols in Molecular, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994). Briefly, 1 microliter of ligation reaction was mixed with 50 microliters of electrocompetent cells and subjected to a high voltage pulse, after which, samples were incubated in 0.45 milliliters SOC medium (0.5% yeast extract, 2.0 % tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM MgCl2, 10 mM MgSO4 and 20, mM glucose) at 37°C with shaking for 1 hour. Samples were then spread on LB agar plates containing 25 microgram/ml kanamycin sulfate for growth overnight. Transformed colonies of BL21 were then picked and analyzed to evaluate cloned inserts as described below.

Identification of recombinant pET expression plasmids carrying H. pylori sequences

Individual BL21 clones transformed with recombinant pET-28b-H.pylori ORFs were analyzed by PCR amplification of the cloned inserts using the same forward and reverse primers, specific for each *H. pylori* sequence, that were used in the original PCR amplification cloning reactions. Successful amplification verified the integration of the *H. pylori* sequences in the expression vector (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., eds., 1994).

Isolation and Preparation of plasmid DNA from BL21 transformants

Individual clones of recombinant pET-28b vectors carrying properly cloned *H. pylori* ORFs were picked and incubated in 5 mls of LB broth plus 25 microgram/ml kanamycin sulfate overnight. The following day plasmid DNA was isolated and purified using the Qiagen plasmid purification protocol (Qiagen Inc., Chatsworth, CA, USA).

Expression of recombinant H. pylori sequences in E. coli

The pET vector can be propagated in any *E. coli* K-12 strain e.g. HMS174, HB101, JM109, DH5, etc. for the purpose of cloning or plasmid preparation. Hosts for expression include *E. coli* strains containing a chromosomal copy of the gene for T7 RNA polymerase. These hosts are lysogens of bacteriophage DE3, a lambda derivative that carries the lacI gene, the lacUV5 promoter and the gene for T7 RNA polymerase. T7 RNA polymerase is induced by addition of isopropyl-B-D-thiogalactoside (IPTG), and the T7 RNA polymerase transcribes any target plasmid, such as pET-28b, carrying a T7 promoter and a gene of interest. Strains used include: BL21(DE3) (Studier, F.W., Rosenberg, A.H., Dunn, J.J., and Dubendorff, J.W. (1990) Meth. Enzymol. 185, 60-89).

To express recombinant *H. pylori* sequences, 50 nanograms of plasmid DNA isolated as described above was used to transform competent BL21(DE3) bacteria as described above (provided by Novagen as part of the pET expression system kit). The lacZ gene (beta-galactosidase) was expressed in the pET-System as described for the *H. pylori* recombinant constructions. Transformed cells were cultured in SOC medium for 1 hour, and the culture was then plated on LB plates containing 25 micrograms/ml kanamycin sulfate. The following day, bacterial colonies were pooled and grown in LB medium containing kanamycin sulfate (25 micrograms/ml) to an optical density at 600 nM of 0.5 to 1.0 O.D. units, at which point, 1 millimolar IPTG was added to the culture for 3 hours to induce gene expression of the *H. pylori* recombinant DNA constructions.

After induction of gene expression with IPTG, bacteria were pelleted by centrifugation in a Sorvall RC-3B centrifuge at 3500 x g for 15 minutes at 4°C. Pellets were resuspended in 50 milliliters of cold 10 mM Tris-HCl, pH 8.0, 0.1 M NaCl and 0.1 mM EDTA (STE buffer). Cells were then centrifuged at 2000 x g for 20 min at 4°C. Wet pellets were weighed and frozen at -80°C until ready for protein purification.

# III. Purification of recombinant proteins from E. coli Analytical Methods

The concentrations of purified protein preparations were quantified spectrophotometrically using absorbance coefficients calculated from amino acid

content (Perkins, S.J. 1986 Eur. J. Biochem. 157, 169-180). Protein concentrations were also measured by the method of Bradford, M.M. (1976) Anal. Biochem. 72, 248-254, and Lowry, O.H., Rosebrough, N., Farr, A.L. & Randall, R.J. (1951) J. Biol. Chem. 193, pages 265-275, using bovine serum albumin as a standard.

SDS-polyacrylamide gels (12% or 4.0 to 25 % acrylamide gradient gels) were purchased from BioRad (Hercules, CA, USA), and stained with Coomassie blue. Molecular weight markers included rabbit skeletal muscle myosin (200 kDa), *E. coli* (galactosidase (116 kDa), rabbit muscle phosphorylase B (97.4 kDa), bovine serum albumin (66.2 kDa), ovalbumin (45 kDa), bovine carbonic anhydrase (31 kDa), soybean trypsin inhibitor (21.5 kDa), egg white lysozyme (14.4 kDa) and bovine aprotinin (6.5 kDa).

# 1. Purification of soluble proteins

All steps were carried out at 4°C. Frozen cells were thawed, resuspended in 5 volumes of lysis buffer (20 mM Tris, pH 7.9, 0.5 M NaCl, 5 mM imidazole with 10% glycerol, 0.1 % 2-mercaptoethanol, 200 µg/ ml lysozyme, 1 mM phenylmethylsulfonyl fluoride (PMSF), and 10 µg/ml each of leupeptin, aprotinin, pepstatin, L-1-chloro-3-[4-tosylamido]-7-amino-2-heptanone (TLCK), L-1-chloro-3-[4-tosylamido]-4-phenyl-2-butanone (TPCK), and soybean trypsin inhibitor, and ruptured by several passages through a small volume microfluidizer (Model M-110S, Microfluidics International Corporation, Newton, MA). The resultant homogenate was made 0.1 % Brij 35, and centrifuged at 100,000 x g for 1 hour to yield a clear supernatant (crude extract).

Following filtration through a 0.8 μm Supor filter (Gelman Sciences, FRG) the crude extract was loaded directly onto a Ni<sup>2+-</sup> nitrilotriacetate-agarose (NTA) with a 5 milliliter bed volume (Hochuli, E., Dbeli, H., and Schacheer, A. (1987) J. Chromatography 411, 177-184) pre-equilibrated in lysis buffer containing 10 % glycerol, 0.1 % Brij 35 and 1 mM PMSF. The column was washed with 250 ml (50 bed volumes) of lysis buffer containing 10 % glycerol, 0.1 % Brij 35, and was eluted with sequential steps of lysis buffer containing 10 % glycerol, 0.05 % Brij 35, 1 mM PMSF, and 20, 100, 200, and 500 mM imidazole in succession. Fractions were monitored by absorbance at OD<sub>280</sub> nm, and peak fractions were analyzed by SDS-PAGE. Fractions containing the recombinant protein eluted at 100 mM imidazole.

Recombinant protein 14640637 and proteins, beta-galactosidase (lacZ) and peptidyl-prolyl cis-trans isomerase (ppiB)

Fractions containing the recombinant proteins from the Ni<sup>2+</sup>-NTA-agarose columns were pooled and then concentrated to approximately 5 ml by centrifugal

filtration (Centriprep-10, Amicon, MA), and loaded directly onto a 180-ml column (1.6 X 91 cm) of Sephacryl S-100 HR gel filtration medium equilibrated in Buffer A (10 mM Hepes, pH 7.5, 150 mM NaCl, 0.1 mM EGTA) and run in Buffer A at 18 ml/h. Fractions containing the recombinant protein were identified by absorbance at 280 nm and analyzed by SDS-PAGE. Fractions were pooled and concentrated by centrifugal filtration.

# Recombinant protein 7116626

Fractions containing the recombinant protein from the Ni<sup>2+</sup>-NTA-agarose column were pooled and dialyzed overnight against 1 liter of dialysis buffer (10 mM MOPS, pH 6.5, 50 mM NaCl, 0.1 mM EGTA, 0.02% Brij 35 and 1 mM PMSF). In the morning, a fine white precipitate was removed by centrifugation and the resulting supernatant was loaded onto an 8 ml (8 x 75 mm) MonoS high performance liquid chromatography column (Pharmacia Biotechnology, Inc., Piscataway, NJ, USA) equilibrated in buffer B (10 mM MOPS, pH 6.5, 0.1 mM EGTA) containing 50 mM NaCl. The column was washed with 10 bed volumes of buffer B containing 50 mM NaCl, and developed with a 50-ml linear gradient of increasing NaCl (50 to 500 mM). Recombinant protein 7116626 eluted as a sharp peak at 300 mM NaCl.

## 2. Purification of insoluble proteins from inclusion bodies

The following steps were carried out at 4°C. Cell pellets were resuspended in lysis buffer with 10% glycerol 200 µg/ ml lysozyme, 5 mM EDTA, 1mM PMSF and 0.1% -mercaptoethanol. After passage through the cell disrupter, the resulting homogenate was made 0.2% deoxycholate, stirred 10 minutes, then centrifuged at 20,000 x g, for 30 min. The pellets were washed with lysis buffer containing 10% glycerol, 10 mM EDTA, 1% Triton X-100, 1 mM PMSF and 0.1% -mercaptoethanol, followed by several washes with lysis buffer containing 1 M urea, 1 mM PMSF and 0.1% 2-mercaptoethanol. The resulting white pellet was composed primarily of inclusion bodies, free of unbroken cells and membranous materials...

#### Recombinant proteins 26054702, 16225006, 30100332, 4721061

The following steps were carried out at room temperature. Purified inclusion bodies were dissolved in 20 ml 8.0 M urea in lysis buffer with 1 mM PMSF and 0.1 % 2-mercaptoethanol, and incubated at room temperature for 1 hour. Materials that did not dissolve were removed by centrifugation. The clear supernatant was filtered, then loaded onto a Ni<sup>2+</sup>-NTA agarose column pre-equilibrated in 8.0 M urea in Lysis Buffer. The column was washed with 250 ml (50 bed volumes) of lysis buffer

25

30

containing 8 M urea, 1.0 mM PMSF and 0.1 % 2-mercaptoethanol, and developed with sequential steps of lysis buffer containing 8M urea, 1 mM PMSF, 0.1 % 2-mercaptoethanol and 20, 100, 200, and 500 mM imidazole in succession. Fractions were monitored by absorbance at OD<sub>280</sub> nm, and peak fractions were analyzed by SDS-PAGE. Fractions containing the recombinant protein eluted at 100 mM imidazole.

## Recombinant proteins 29479681, 26380318

The pellet containing the inclusion bodies was solubilized in buffer B containing 8 M urea, 1 mM PMSF and 0.1 % 2-mercaptoethanol, and incubated for 1 hour at room temperature. Insoluble materials were removed by centrifugation at 20,000 x g for 30 min, and the cleared supernatant was loaded onto a 15 ml (1.6 x 7.5 cm) SP-Sepharose column pre-equilibrated in buffer B, 6 M urea, 1 mM PMSF, 0.1 % 2-mercaptoethanol. After washing the column with 10 bed volumes, the column was developed with a linear gradient from 0 to 500 mM NaCl.

15 Dialysis and concentration of protein samples

Urea was removed slowly from the protein samples by dialysis against Trisbuffered saline (TBS; 10 mM Tris pH 8.0, 150 mM NaCl) containing 0.5 % deoxycholate (DOC) with sequential reduction in urea concentration as follows; 6M, 4M, 3M, 2M, 1M, 0.5 M and finally TBS without any urea. Each dialysis step was conducted for a minimum of 4 hours at room temperature.

After dialysis, samples were concentrated by pressure filtration using Amicon stirred-cells. Protein concentrations were measured using the methods of Perkins (1986 Eur. J. Biochem. 157, 169-180), Bradford ((1976) Anal. Biochem. 72, 248-254) and Lowry ((1951) J. Biol. Chem. 193, pages 265-275).

The recombinant proteins purified by the methods described above are summarized in Table 4 below.

#### TABLE 4

J99 Sequence Identifier  Outer Memb	Homolog identified by Blast prane Protein	Gene symbol of Homolog	Bacterial cell fraction used to purify recombinant proteins	Method of purification	Relative MW on SDS- PAGE gel	Final concentratio n of purified protein	Composit ionof buffer
16225006	P28635	YEAC	Inclusion bodies	His-Tag	18 kDa	5 mg/ml	В
26054702	P15929	flgH	Inclusion bodies	His-Tag	37 kDa	1.18 mg/ml	В

	r ·	<u> </u>	T	<u> </u>	1		oo day.
							as dry pellet
<u> </u>		<del> </del>					pener
7116626	P26093	e(P4)	Soluble fraction	His-Tag	29 kDa	0.8 mg/ml	A
7110020	120033	1 5(- 1)	Soldole Haction	This-Tag	27 KDa	1.85 mg/mi	C
· · · · · · · · · · · · · · · · · · ·		<del> </del>				1.03 lilg/lill	
29479681	P13036	fecA	Inclusions	SP-	23 kDa	2.36 mg/ml	В
25475001	1 13030	l lech	bodies	Sepharose	23 KDa	2.30 mg/m	Þ
	<u> </u>	<del> </del>	Doules	Sepharose		0.5 mg ml	В
		<del> </del>	<del> </del>			U.J ing ini	as dry
		İ	·	ļ		<del></del>	pellet
	·	<del> </del>	<del> </del>				pener
14640637	P16665	TPF1	Soluble fraction	His-Tag	17 kDa	2.4 mg/ml	A
11010051	1.0002		Soluble Haction		ion S100 HR		Λ
		<u> </u>		germuat	1011 3100 11K		
Perinlasmic/	Secreted Pro	tein .	1	L	Ĺ		
- cripiasiiiO	Jecieta i IU	1	1	<del></del>	T	· · · · · · · · · · · · · · · · · · ·	
3010032	P23847	dppA	Inclusion bodies	Uio Too	LILIDa	2.00 / 1	
3010032	123047	ирри	menusion bodies	His-Tag	11 kDa	2.88 mg/ml	В
4721061	P36175	GCP	Inclusion bodies	His Ts	201-5-	20 / 1	
4/21001	F30173	GCF	inclusion bodies	His-Tag	38 kDa	2.8 mg/ml	В
Other Surfac	Duotoina	<u> </u>	L			i	
Other Suriat	e Froteins	<del> </del>			T		
4821082	P08089	24	7				
4821082	PUSUSS	M	Inclusion bodies	His-Tag	20 kDa	1.16 mg/ml	В
		protein		· · · ·			
978477	L28919	FBP54	In along to the	GD.	4415	266 ( )	
9/64//	L20919	FBF54	Inclusion bodies	SP-	44 kDa	2.56 mg/ml	В
				Sepharose		0.2 (: 1	
Inner Memb	mana Protoina	<u></u>	l			0.3 mg/ml	В
Inner Memb	rane r rotein	<u>,                                      </u>	·	<del></del>			-
26380318	P15933	NiG	Inclusion hadian	CD	11110	22 / 1	<u> </u>
20380318	P13933	l ing	Inclusion bodies	SP-	11 kDa	22 mg/ml	В
	· · · · · · · · · · · · · · · · · · ·	<del> </del>		Sepharose			
·							
Control Prot	oing swith His	Too	·				
Control Prot	eins with Fils	- 1 ag	T .				
-	P00722	lo = 77	Calubia C	11:- 0	11615	10	
· .	FUU/ZZ	lacZ	Soluble fraction	His-Tag	116 kDa	10 mg/ml	Α
		<del> </del>	·	gei filtrati	on S200 HR		
	<del></del>		C-1-h1-C	771	04.15		
		ppiB	Soluble fraction	His-Tag	21 kDa	4.4 mg/ml	A
. D C				gel filtrati	on S100 HR		
Buffer	-		•				
composition						.	
· s:	·						
			Cl, 0.1 mM EGTA				
B= 10 mM Tr							
C= 10 mM M	OPS pH 6.5, 1	300 mM N	aCl, 0.1 EGTA			_1	

# IV. Analysis of H. pylori proteins as Vaccine candidates

To investigate the immunomodulatory effect of *H. pylori* proteins, a mouse/*H. pylori* model was used. This model mimics the human *H. pylori* infection in many respects. The focus is on the effect of oral immunization in *H. pylori* infected animals in order to test the concept of therapeutic oral immunotherapy.

#### Animals

5

10

15

20

25

35

Female SPF BALB/c mice were purchased from Bomholt Breeding center (Denmark). They were kept in ordinary makrolon cages with free supply of water and food. The animals were 4-6 weeks old at arrival.

Infection

After a minimum of one week of acclimatization, the animals were infected with a type 2 strain (VacA negative) of *H. pylori* (strain 244, originally isolated from an ulcer patient). In our hands, this strain has earlier proven to be a good colonizer of the mouse stomach. The bacteria were grown overnight in Brucella broth supplemented with 10 % fetal calf serum, at 37°C in a microaerophilic atmosphere (10% CO<sub>2</sub>, 5%O<sub>2</sub>). The animals were given an oral dose of omeprazole (400 µmol/kg) and 3-5 h after this an oral inoculation of *H. pylori* in broth (approximately 10<sup>8</sup> cfu/animal). Positive take of the infection was checked in some animals 2-3 weeks after the inoculation.

Antigens

Recombinant *H. pylori* antigens were chosen based on their association with externally exposed *H. pylori* cell membrane. These antigens were selected from the following groups: (1.) Outer Membrane Proteins; (2.) Periplastic/Secreted proteins; (3.) Outer Surface proteins; and (4.) Inner Membrane proteins. All recombinant proteins were constructed with a hexa-HIS tag for purification reasons and the non-*Helicobacter pylori* control protein (b-galactosidase from *E. coli*; LacZ), was constructed in the same way.

All antigens were given in a soluble form, i.e. dissolved in either a HEPES buffer or in a buffer containing 0.5% Deoxycholate (DOC).

The antigens are listed in Table 5 below.

<u>Table 5</u>
<u>Helicobacter pylori proteins</u>

Outer membrane Proteins Protein 7116626 Protein 4721061 Protein 16225006 Protein 29479681 Protein 14640637

## 5 Periplasmic/Secreted Proteins

Protein 30100332

## Other cell envelope proteins

Protein 4821082

10

20

# Flagella-associated proteins

Protein 26380318

#### **Control proteins**

15 b-galactosidase (LacZ)

#### *Immunizations*

Ten animals in each group were immunized 4 times over a 34 day period (day 1, 15, 25 and 35). Purified antigens in solution or suspension were given at a dose of 100 mg/mouse. As an adjuvant, the animals were also given 10 µg/mouse of Cholera toxin (CT) with each immunization. Omeprazole (400 mmol/kg) was given orally to the animals 3-5 h prior to immunization as a way of protecting the antigens from acid degradation. Infected control animals received HEPES buffer + CT or DOC buffer + CT. Animals were sacrificed 2-4 weeks after final immunization. A general outline of the study is shown in Table 6 below.

<u>Table 6</u>
<u>Study outline, therapeutic immunization:</u>

30

25

Mice were all infected with H. pylori strain Ah244 at day 30.

35	Substance	Mouse strain n=10	Dose/mouse	Dates for dosing
	1. Controls, PBS	Balb/c	0.3 ml	0, 14, 24, 34
	2. Cholera toxin, 10 μg	Balb/c	0.3 ml	0, 14, 24, 34
40	3. Protein 16225006, 100 μg + CT 1	0 μg Balb/c	0.3 ml	0, 14, 24, 34
	4. Protein 26054702, 100 μg + CT 1	0 μg Balb/c	0.3 ml	0, 14, 24, 34

	5. Protein 26380318, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
-	6. Protein 29479681, $100 \mu g + CT 10 \mu g Balb/c$	0.3 ml	0, 14, 24, 34
5	7. Protein 30100332, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
•	8. Protein 4721061, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
10	9. Protein 4821082, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
	10. Protein 7116626, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34
	11.Protein 14640637, 100 μg + CT 10 μg Balb/c	0.3 ml	0, 14, 24, 34

#### 15 Analysis of infection

20

25

30

35

Mucosal infection: The mice were sacrificed by CO<sub>2</sub> and cervical dislocation. The abdomen was opened and the stomach removed. After cutting the stomach along the greater curvature, it was rinsed in saline. The mucosa from the antrum and corpus of an area of 25mm<sup>2</sup> was scraped separately with a surgical scalpel. The mucosa scraping was suspended in Brucella broth and plated onto Blood Skirrow selective plates. The plates were incubated under microaerophilic conditions for 3-5 days and the number of colonies was counted. The identity of *H. pylori* was ascertained by urease and catalase test and by direct microscopy or Gram staining.

The urease test was performed essentially as follows. The reagent, Urea Agar Base Concentrate, was purchased from DIFCO Laboratories, Detroit, MI (Catalog # 0284-61-3). Urea agar base concentrate was diluted 1:10 with water. 1 ml of if the diluted concentrate was mixed with 100-200 ml of actively growing *H. pylori* cells. Color change to magenta indicated that cells were urease positive.

The catalase test was performed essentially as follows. The reagent, N,N,N',N'-Tetramethyl-p-Phenylenediamine, was purchased from Sigma, St. Louis, MO (Catalog # T3134). A solution of the regent (1% w/v in water) was prepared. *H. pylori* cells were swabbed onto Whatman filter paper and overlaid with the 1% solution. Color change to dark blue indicated that the cells were catalase positive.

<u>Serum antibodies:</u> From all mice serum was prepared from blood drawn by heart puncture. Serum antibodies were identified by regular ELISA techniques, where the specific antigens of *Helicobacter pylori* were plated.

Mucosal antibodies: Gentle scrapings of a defined part of the corpus and of 4 cm of duodenum were performed in 50% of the mice in order to detect the presence of

antibodies in the mucous. The antibody titers were determined by regular ELISA technique as for serum antibodies.

Statistical analysis: Wilcoxon-Mann-Whitney sign rank test was used for determination of significant effects of the antigens on *Helicobacter pylori* colonization. P<0.05 was considered significant. Because the antrum is the major colonization site for *Helicobacter* most emphasis was put upon changes in the antral colonization.

#### Results

5

10

15

20

25

Antibodies in sera: All antigens tested given together with CT gave rise to a measurable specific titer in serum. The highest responses were seen with Protein 7116626, Protein 4721061, Protein 26380318, Protein 14640637 and Protein 4821082 (see Figure 1).

Antibodies in mucus: In the mucus scrapings, specific antibodies against all antigens tested were seen. By far the strongest response was seen with Protein 30100332, followed by Protein 14640637, and Protein 26380318 (see Figure 2).

#### Therapeutic immunization effects:

All control animals (BALB/c mice) were well colonized with *H. pylori* (strain AH244) in both antrum and corpus of the stomach. Of the antigens tested 3 proteins (Protein 4721061, Protein 4821082, and Protein 14640637) gave a good and significant reduction and/or eradication of the *H. pylori* infection. The degree of colonization of the antrum was lower following immunization with Protein 7116626 and Protein 26380318 compared to control. The effect of Proteins 16225006, 29479681, and 30100332 did not differ from control. The control protein lacZ, i.e. the non-*H. pylori* protein, had no eradication effect and in fact had higher *Helicobacter* colonization compared to the HEPES + CT control. All data are shown in Figures 3 and 4 for proteins dissolved in HEPES and DOC respectively. Data is shown as geometric mean values. n=8-10 Wilcoxon-Mann-Whitney sign rank test \* = p<0.05; x/10 = number of mice showing eradication of *H. pylori* over the total number of mice examined.

30

35

The data presented indicate that all of the *H. pylori* associated proteins included in this study, when used as oral immunogens in conjunction with the oral adjuvant CT, resulted in stimulation of an immune response as measured by specific serum and mucosal antibodies. A majority of the proteins led to a reduction, and in some cases complete clearance of the colonization of *H. pylori* in this animal model. It should be noted that the reduction or clearance was due to heterologous protection rather than homologous protection (the polypeptides were based on the *H. pylori* J99 strain

sequence and used in the therapeutic immunization studies against a different (AH244) challenge strain, indicating the vaccine potential against a wide variety of *H. pylori* strains.

The highest colonization in the antrum was seen in animals treated with the non-Helicobacter protein LacZ, indicating that the effects seen with the Helicobacter pylori antigens were specific.

Taken together these data strongly support the use of these *H. pylori* proteins in a pharmaceutical formulation for the use in humans to treat and/or prevent *H. pylori* infections.

10

15

20

25

30

35

# V. Sequence Variance Analysis of genes in Helicobacter pylori strains

Four genes were cloned and sequenced from several strains of *H. pylori* to compare the DNA and deduced amino acid sequences. This information was used to determine the sequence variation between the *H. pylori* strain, J99, and other *H. pylori* strains isolated from human patients.

## Preparation of Chromosomal DNA.

Cultures of *H. pylori* strains (as listed in Table 9) were grown in BLBB (1% Tryptone, 1% Peptamin 0.1% Glucose, 0.2% Yeast Extract 0.5% Sodium Chloride, 5% Fetal Bovine Serum) to an OD<sub>600</sub> of 0.2. Cells were centrifuged in a Sorvall RC-3B at 3500 x g at 4°C for 15 minutes and the pellet resuspended in 0.95 mls of 10 mM Tris-HCl, 0.1 mM EDTA (TE). Lysozyme was added to a final concentration of 1mg/ml along with, SDS to 1% and RNAse A + T1 to 0.5mg/ml and 5 units/ml respectively, and incubated at 37°C for one hour. Proteinase K was then added to a final concentration of 0.4mg/ml and the sample was incubated at 55 C for more than one hour. NaCl was added to the sample to a concentration of 0.65 M, mixed carefully, and 0.15 ml of 10% CTAB in 0.7M NaCL (final is 1% CTAB/70mM NaCL) was added followed by incubation at 65°C for 20 minutes. At this point, the samples were extracted with chloroform:isoamyl alcohol, extracted with phenol, and extracted again with chloroform:isoamyl alcohol. DNA was precipitated with either EtOH (1.5 x volumes) or isopropanol (0.6 x volumes) at -70°C for 10minutes, washed in 70% EtOH and resuspended in TE.

### PCR Amplification and cloning.

Genomic DNA prepared from twelve strains of *Helicobacter pylori* was used as the source of template DNA for PCR amplification reactions (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). To

amplify a DNA sequence containing an *H. pylori* ORF, genomic DNA (10 nanograms) was introduced into a reaction vial containing 2 mM MgCl<sub>2</sub>, 1 micromolar synthetic oligonucleotide primers (forward and reverse primers, see Table 7) complementary to and flanking a defined *H. pylori* ORF, 0.2 mM of each deoxynucleotide triphosphate; dATP, dGTP, dCTP, dTTP and 0.5 units of heat stable DNA polymerase (Amplitaq, Roche Molecular Systems, Inc., Branchburg, NJ, USA) in a final volume of 20 microliters in duplicate reactions.

Table 7

Oligonucleotide primers used for PCR amplification of H. pylori DNA sequences.

Outer membrane	Forward primer 5' to 3'	Reverse Primer 5' to 3'
Proteins		
<b>Protein 26054702</b> (for	5'-	5'-
strains AH4, AH15,	TTAACCATGGTGAAA	TAGAATTCGCCTCTA
AH61, 5294, 5640,	AGCGATA-3' (SEQ ID	AAACTTTAG-3' (SEQ
AH18, and AH244)	NO:169)	ID NO:170)
	<b>.</b>	
Protein 26054702	5'-	5'-
(for strains AH5, 5155,	TTAACCATGGTGAAA	TAGAATTCGCATAAC
7958, AH24, and J99)	AGCGATA-3' (SEQ ID	GATCAATC-3' (SEQ ID
	NO:171)	NO:172)
D # 511//2/	c.	
Protein 7116626	5'-	5'-
	ATATCCATGGTGAGT	ATGAATTCAATTTTT
	TTGATGA-3' (SEQ ID	TATTTTGCCA-3' (SEQ
	NO:173)	ID NO:174)
Protein 29479681	5'-	5'-
	AATTCCATGGCTATC	ATGAATTCGCCAAAA
	CAAATCCG-3' (SEQ ID	TCGTAGTATT-3' (SEQ
	NO:175)	ID NO:176)
Protein 346	5'-	5'-
	GATACCATGGAATTT	TGAATTCGAAAAAGT
·	ATGAAAAAG-3' (SEQ	GTAGTTATAC-3' (SEQ
	ID NO:177)	ID NO:178)

The following thermal cycling conditions were used to obtain amplified DNA products for each ORF using a Perkin Elmer Cetus/ GeneAmp PCR System 9600 thermal cycler:

Protein 7116626 and Protein 346;

Denaturation at 94°C for 2 min,

2 cycles at 94°C for 15 sec, 30°C for 15 sec and 72°C for 1.5 min

23 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min

Reactions were concluded at 72°C for 6 minutes.

Protein 26054702 for strains AH5, 5155, 7958, AH24, and J99; Denaturation at 94°C for 2 min,

2 cycles at 94°C for 15 sec, 30°C for 15 sec and 72°C for 1.5 min 25 cycles at 94°C for 15 sec, 55°C for 15 sec and 72°C for 1.5 min Reaction was concluded at 72°C for 6 minutes.

Protein 26054702 and Protein 294796813 for strains AH4, AH15, AH61, 5294, 5640,

15 AH18, and Hp244;

Denaturation at 94°C for 2 min, 2 cycles at 94°C for 15 sec, 30°C for 20 sec and 72°C for 2 min 25 cycles at 94°C for 15 sec, 55°C for 20 sec and 72°C for 2 min Reactions were concluded at 72°C for 8 minutes.

20

35

Upon completion of thermal cycling reactions, each pair of samples were combined and used directly for cloning into the pCR cloning vector as described below.

Cloning of H. pylori DNA sequences into the pCR TA cloning vector.

All amplified inserts were cloned into the pCR 2.1 vector by the method described in the Original TA cloning kit (Invitrogen, San Diego, CA). Products of the ligation reaction were then used to transform the TOP10F' (INVaF' in the case of H. pylori sequence 350) strain of E. coli as described below.

30 Transformation of competent bacteria with recombinant plasmids

Competent bacteria, *E coli* strain TOP10F' or *E. coli* strain INVaF' were transformed with recombinant pCR expression plasmids carrying the cloned *H. pylori* sequences according to standard methods (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). Briefly, 2 microliters of 0.5 micromolar BME was added to each vial of 50 microliters of competent cells. Subsequently, 2 microliters of ligation reaction was mixed with the competent cells and incubated on ice for 30 minutes. The cells and ligation mixture were then subjected to a

"heat shock" at 42°C for 30 seconds, and were subsequently placed on ice for an additional 2 minutes, after which, samples were incubated in 0.45 milliliters SOC medium (0.5% yeast extract, 2.0 % tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM MgCl2, 10 mM MgSO4 and 20, mM glucose) at 37°C with shaking for 1 hour. Samples were then spread on LB agar plates containing 25 microgram/ml kanamycin sulfate or 100 micrograms/ml ampicillan for growth overnight. Transformed colonies of TOP10F' or INVaF' were then picked and analyzed to evaluate cloned inserts as described below. Identification of recombinant PCR plasmids carrying H. pylori sequences

Individual TOP10F' or INVaF' clones transformed with recombinant pCR-H.pylori ORFs were analyzed by PCR amplification of the cloned inserts using the same forward and reverse primers, specific for each H. pylori sequence, that were used in the original PCR amplification cloning reactions. Successful amplification verified the integration of the H. pylori sequences in the cloning vector (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994).

Individual clones of recombinant pCR vectors carrying properly cloned *H. pylori* ORFs were picked for sequence analysis. Sequence analysis was performed on ABI Sequencers using standard protocols (Perkin Elmer) using vector-specific primers (as found in PCRII or pCR2.1, Invitrogen, San Diego, CA) and sequencing primers specific to the ORF as listed in Table 8 below.

10

15

<u>Table 8</u>
<u>Oligonucleotide primers used for sequencing of H. pylori DNA sequences.</u>

Outer membrane	Forward primers 5' to 3'	Reverse Primers 5' to 3'
Proteins		
	- X -	
Protein 26054702	5'-	5'-
	CCCTTCATTTTAGAAATC	CTTTGGGTAAAAACGCA
	G-3' (SEQ ID NO:179)	TC-3' (SEQ ID NO:186)
	5'-	5'-
	ATTTCAACCAATTCAAT	CGATCTTTGATCCTAATT
	GCG-3' (SEQ ID NO:180)	CA-3' (SEQ ID NO:187)
	5'-	5'-
	GCCCCTTTTGATTTGAAG	ATCAAGTTGCCTATGCT
	CT-3' (SEQ ID NO:181)	GA-3' (SEQ ID NO:188)
·	5'-	
	TCGCTCCAAGATACCAA	
	GAAGT-3' (SEQ ID	
	NO:182)	
	5'-	
f'n	CTTGAATTAGGGGCAAA	
	GATCG-3' (SEQ ID	
	NO:183)	
	5'-	
	ATGCGTTTTTACCCAAA	
	GAAGT-3' (SEQ ID	
	NO:184)	
	5'-	
	ATAACGCCACTTCCTTAT	
	TGGT-3' (SEQ ID NO:185)	
D.,.4.: 5116606		
Protein 7116626	5'-	5'-
	TTGAACACTTTTGATTAT	GTCTTTAGCAAAAATGG
	GCGG-3' (SEQ ID NO:189)	CGTC-3' (SEQ ID NO:191)
	S'-	5'-
·	GGATTATGCGATTGTTTT	AATGAGCGTAAGAGAGC
- ,	ACAAG-3' (SEQ ID NO:190)	CTTC-3' (SEQ ID NO:192)
Protein	5'-	5'-
29479681	CTTATGGGGGTATTGTC	•
47717U01	A-3' (SEQ ID NO:193)	AGGTTGTTGCCTAAAGA
	5'-	CT-3' (SEQ ID NO:195) 5'-
	AGCATGTGGGTATCCAG	
	C-3' (SEQ ID NO:194)	CTGCCTCCACCTTTGATC
<del></del>	C-3 (3EQ ID NO:194)	-3' (SEQ ID NO:196)

Protein 346	5'- ACCAATATCAATTGGCA CT-3' (SEQ ID NO:197) 5'- ACTTGGAAAAGCTCTGC A-3' (SEQ ID NO:198)	5'- CTTGCTTGTCATATCTAG C-3' (SEQ ID NO:199) 5'- GTTGAAGTGTTGGTGCT A-3' (SEQ ID NO:200)
	5'- CAAGCAAGTGGTTTGGT TTTAG-3' (SEQ ID NO:201) 5'- TGGAAAGAGCAAATCAT TGAAG-3' (SEQ ID NO:202)	5'- GCCCATAATCAAAAAGC CCAT-3' (SEQ ID NO:203) 5'- CTAAAAACCAAACCACTT GCT TGTC-3' (SEQ ID NO:204)
Vector Primers	5'- GTAAAACGACGGCCAG- 3' (SEQ ID NO:205)	5'- CAGGAAACAGCTATGAC -3' (SEQ ID NO:206)

#### Results

10

15

20

To establish the PCR error rate in these experiments, five individual clones of Protein 26054702, prepared from five separate PCR reaction mixtures from *H. pylori* strain J99, were sequenced over a total length of 897 nucleotides for a cumulative total of 4485 bases of DNA sequence. DNA sequence for the five clones was compared to a DNA sequence obtained previously by a different method, i.e., random shotgun cloning and sequencing. The PCR error rate for the experiments described herein was determined to be 2 base changes out of 4485 bases, which is equivalent to an estimated error rate of less than or equal to 0.04%.

DNA sequence analysis was performed on four different open reading frames identified as genes and amplified by PCR methods from a dozen different strains of the bacterium *Helicobacter pylori*. The deduced amino acid sequences of three of the four open reading frames that were selected for this study showed statistically significant BLAST homology to defined proteins present in other bacterial species. Those ORFs included: Protein 26054702, homologous to the val A & B genes encoding an ABC transporter in F. novicida; Protein 7116626, homologous to lipoprotein e (P4) present in the outer membrane of H. influenzae; Protein 29479681, homologous to fecA, an outer membrane receptor in iron (III) dicitrate transport in *E. coli*. Protein 346 was identified as an unknown open reading frame, because it showed low homology with sequences in the public databases.

To assess the extent of conservation or variance in the ORFs across various strains of *H. pylori*, changes in DNA sequence and the deduced protein sequence were compared to the DNA and deduced protein sequences found in the J99 strain of *H*.

pylori (see Table 9 below). Results are presented as percent identity to the J99 strain of H. pylori sequenced by random shotgun cloning. To control for any variations in the J99 sequence each of the four open reading frames were cloned and sequenced again from the J99 bacterial strain and that sequence information was compared to the sequence information that had been collected from inserts cloned by random shotgun sequencing of the J99 strain. The data demonstrate that there is variation in the DNA sequence ranging from as little as 0.12 % difference (Protein 346, J99 strain) to approximately 7% change (Protein 26054702, strain AH5). The deduced protein sequences show either no variation ( Protein 346, strains AH18 and AH24) or up to as much as 7.66% amino acid changes (Protein 26054702, Strain AH5).

Table 9

15	Multiple Strain DNA Sequence analysis of H. pylori Vaccine Candidates								
13	J99 Protein #:	26054702	2054702	7116626 7	116626 2	9479681	294 <b>79</b> 681	346 3	46
20	Length of Regi Sequenced:		746 nt. 2	32 a.a.	96 nt.	182 a.a.	548 nt. 2	73 a.a. 81	9 nt.
	Strain Tested	AA identity	Nuc.	AA identity	Nuc.	AA identity	Nuc.	AA identity	Nuc.
	J99	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	99.63%	99.88%
	AH244	95.16%	95.04%	n.d.	n.d.	99.09%	96.71%	98.90%	96.45%
	AH4	95.97%	95.98%	97.84%	95.83%	n.d.	n.d.	97.80%	95.73%
	AH5	92.34%	93.03%	98.28%	96.12%	98.91%	96.90%	98.53%	95.73%
	AH15	95.16%	94.91%	97.41%	95.98%	99.82%	97.99%	99.63%	96.09%
	AH61	n.d.	n.d.	97.84%	95.98%	99.27%	97.44%	n.d.	n.d.
•	5155	n.d.	n.d.	n.d.	n.đ.	99.45%	97.08%	98.53%	95.60%
	5294	94.35%	94.37%	98.28%	95.40%	99.64%	97.26%	97.07%	95.48%
	7958	94.35%	94.10%	97.84%	95.40%	n.d.	n.d.	99.63%	96.46%
	5640	95.16%	94.37%	97.41%	95.69%	99.09%	97.63%	98.53%	95.48%
	AH18	n.d.	n.d.	98.71%	95.69%	99.64%	97.44%	100.00%	95.97%
	AH24	94.75%	95.04%	97.84%	95.40%	99.27%	96.71%	100.00%	96.46%

n.d.= not done.

15

20

25

30

35

# VI. Experimental Knock-Out Protocol for the Determination of Essential H. pylori Genes as Potential Therapeutic Targets

Therapeutic targets are chosen from genes whose protein products appear to play key roles in essential cell pathways such as cell envelope synthesis, DNA synthesis, transcription, translation, regulation and colonization/virulence.

The protocol for the deletion of portions of *H. pylori* genes/ORFs and the insertional mutagenesis of a kanamycin-resistance cassette in order to identify genes which are essential to the cell is modified from previously published methods (Labigne-Roussel et al., 1988, J. Bacteriology 170, pp. 1704-1708; Cover et al., 1994, J. Biological Chemistry 269, pp. 10566-10573; Reyrat et al., 1995, Proc. Natl. Acad. Sci. 92, pp 8768-8772). The result is a gene "knock-out."

### Identification and Cloning of H. pylori Gene Sequences

The sequences of the genes or ORFs (open reading frames) selected as knock-out targets are identified from the *H. pylori* genomic sequence and used to design primers to specifically amplify the genes/ORFs. All synthetic oligonucleotide primers are designed with the aid of the OLIGO program (National Biosciences, Inc., Plymouth, MN 55447, USA), and can be purchased from Gibco/BRL Life Technologies (Gaithersburg, MD, USA). If the ORF is smaller than 800 to 1000 base pairs, flanking primers are chosen outside of the open reading frame.

Genomic DNA prepared from the *Helicobacter pylori* HpJ99 strain (ATCC 55679; deposited by Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02154) is used as the source of template DNA for amplification of the ORFs by PCR (polymerase chain reaction) (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). For the preparation of genomic DNA from *H. pylori*, see Example I. PCR amplification is carried out by introducing 10 nanograms of genomic HpJ99 DNA into a reaction vial containing 10 mM Tris pH 8.3, 50 mM KCl, 2 mM MgCl<sub>2</sub>, 2 microMolar synthetic oligonucleotide primers (forward=F1 and reverse=R1), 0.2 mM of each deoxynucleotide triphosphate (dATP,dGTP, dCTP, dTTP), and 1.25 units of heat stable DNA polymerase (Amplitaq, Roche Molecular Systems, Inc., Branchburg, NJ, USA) in a final volume of 40 microliters. The PCR is carried out with Perkin Elmer Cetus/GeneAmp PCR System 9600 thermal cyclers.

Upon completion of thermal cycling reactions, each sample of amplified DNA is visualized on a 2% TAE agarose gel stained with Ethidium Bromide (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994) to

15

20

25

30

35

determine that a single product of the expected size had resulted from the reaction. Amplified DNA is then washed and purified using the Qiaquick Spin PCR purification kit (Qiagen, Gaithersburg, MD, USA).

PCR products are cloned into the pT7Blue T-Vector (catalog#69820-1, Novagen, Inc., Madison, WI, USA) using the TA cloning strategy (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). The ligation of the PCR product into the vector is accomplished by mixing a 6 fold molar excess of the PCR product, 10 ng of pT7Blue-T vector (Novagen), 1 microliter of T4 DNA Ligase Buffer (New England Biolabs, Beverly, MA, USA), and 200 units of T4 DNA Ligase (New England Biolabs) into a final reaction volume of 10 microliters. Ligation is allowed to proceed for 16 hours at 16°C.

Ligation products are electroporated (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994) into electroporation-competent XL-1 Blue or DH5-a *E. coli* cells (Clontech Lab., Inc. Palo Alto, CA, USA). Briefly, 1 microliter of ligation reaction is mixed with 40 microliters of electrocompetent cells and subjected to a high voltage pulse (25 microFarads, 2.5 kV, 200 ohms) after which the samples are incubated in 0.45 ml SOC medium (0.5% yeast extract, 2% tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM MgCl<sub>2</sub>, 10 mM MgSO<sub>4</sub> and 20 mM glucose) at 37°C with shaking for 1 hour. Samples are then spread onto LB (10 g/l bacto tryptone, 5 g/l bacto yeast extract, 10 g/l sodium chloride) plates containing 100 microgram/ml of Ampicillin, 0.3% X-gal, and 100 microgram/ml IPTG. These plates are incubated overnight at 37°C. Ampicillin-resistant colonies with white color are selected, grown in 5 ml of liquid LB containing 100 microgram/ml of Ampicillin, and plasmid DNA is isolated using the Qiagen miniprep protocol (Qiagen, Gaithersburg, MD, USA).

To verify that the correct *H.pylori* DNA inserts had been cloned, these pT7Blue plasmid DNAs are used as templates for PCR amplification of the cloned inserts, using the same forward and reverse primers used for the initial amplification of the J99 *H.pylori* sequence. Recognition of the primers and a PCR product of the correct size as visualized on a 2% TAE, ethidium bromide stained agarose gel are confirmation that the correct inserts had been cloned. Two to six such verified clones are obtained for each knock-out target, and frozen at -70°C for storage. To minimize errors due to PCR, plasmid DNA from these verified clones are pooled, and used in subsequent cloning steps.

The sequences of the genes/ORFs are again used to design a second pair of primers which flank the region of *H. pylori* DNA to be either interrupted or deleted (up to 250 basepairs) within the ORFs but are oriented away from each other. The pool of

35

circular plasmid DNAs of the previously isolated clones are used as templates for this round of PCR. Since the orientation of amplification of this pair of deletion primers is away from each other, the portion of the ORF between the primers is not included in the resultant PCR product. The PCR product is a linear piece of DNA with *H. pylori* DNA at each end and the pT7Blue vector backbone between them which, in essence, resultes in the deletion of a portion of the ORFs. The PCR product is visualized on a 1% TAE, ethidium bromide stained agarose gel to confirm that only a single product of the correct size has been amplified.

A Kanamycin-resistance cassette (Labigne-Roussel et al., 1988 J. Bacteriology 170, 1704-1708) is ligated to this PCR product by the TA cloning method used 10 previously (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., F. Ausubel et al., editors, 1994). The Kanamycin cassette containing a Campylobacter kanamycin resistance gene is obtained by carrying out an EcoRI digestion of the recombinant plasmid pCTB8:kan (Cover et al., 1994, J. Biological Chemistry 269, pp. 10566-10573). The proper fragment (1.4 kb) is isolated on a 1% TAE gel, and isolated 15 using the QIAquick gel extraction kit (Qiagen, Gaithersburg, MD, USA). The fragment is end repaired using the Klenow fill-in protocol, which involved mixing 4ug of the DNA fragment, 1 microliter of dATP,dGTP, dCTP, dTTP at 0.5 mM, 2 microliter of Klenow Buffer (New England Biolabs) and 5 units of Klenow DNA Polymerase I Large (Klenow) Fragment (New England Biolabs) into a 20 microliter reaction, incubating at 20 30°C for 15 min, and inactivating the enzyme by heating to 75°C for 10 minutes. This blunt-ended Kanamycin cassette is then purified through a Qiaquick column (Qiagen, Gaithersburg, MD, USA) to eliminate nucleotides. The "T" overhang is then generated by mixing 5 micrograms of the blunt-ended kanamycin cassette, 10 mM Tris pH 8.3, 50 mM KCl, 2 mM MgCl<sub>2</sub>, 5 units of DNA Polymerase (Amplitaq, Roche Molecular 25 Systems, Inc., Branchburg, NJ, USA), 20 microliters of 5 mM dTTP, in a 100 microliter reaction and incubating the reaction for 2 hours at 37°C. The "Kan-T" cassette is purified using a QIAquick column (Qiagen, Gaithersburg, MD, USA). The PCR product of the deletion primers (F2 and R2) is ligated to the Kan-T cassette by mixing 10 to 25 ng of deletion primer PCR product, 50 - 75 ng Kan-T cassette DNA, 1 30 microliter 10x T4 DNA Ligase reaction mixture, 0.5 microliter T4 DNA Ligase (New England Biolabs, Beverly, MA, USA) in a 10 microliter reaction and incubating for 16 hours at 16°C.

The ligation products are transformed into XL-1 Blue or DH5-a *E.coli* cells by electroporation as described previously. After recovery in SOC, cells are plated onto LB plates containing 100 microgram/ml Ampicillin and grown overnight at 37°C. These plates are then replica plated onto plates containing 25 microgram/ml Kanamycin and

10

15

20

25

30

35

allowed to grow overnight. Resultant colonies have both the Ampicillin resistance gene present in the pT7Blue vector, and the newly introduced Kanamycin resistance gene. Colonies are picked into LB containing 25 microgram/ml Kanamycin and plasmid DNA is isolated from the cultured cells using the Qiagen miniprep protocol (Qiagen, Gaithersburg, MD, USA).

Several tests by PCR amplification are conducted on these plasmids to verify that the Kanamycin is inserted in the H. pylori gene/ORF, and to determine the orientation of the insertion of the Kanamycin-resistance gene relative to the H. pylori gene/ORF. To verify that the Kanamycin cassette is inserted into the H. pylori sequence, the plasmid DNAs are used as templates for PCR amplification with the set of primers originally used to clone the H. pylori gene/ORFs. The correct PCR product is the size of the deleted gene/ORF but increased in size by the addition of a 1.4 kilobase Kanamycin cassette. To avoid potential polar effects of the kanamycin resistance cassette on H. pylori gene expression, the orientation of the Kanamycin resistance gene with respect to the knock-out gene/ORF is determined and both orientations are eventually used in H. pylori transformations (see below). To determine the orientation of insertion of the kanamycin resistance gene, primers are designed from the ends of the kanamycin resistance gene ("Kan-1" 5'-ATCTTACCTATCACCTCAAAT-3' (SEQ ID NO:207)), and "Kan-2" 5'-AGACAGCAACATCTTTGTGAA-3' (SEQ ID NO:208)). By using each of the cloning primers in conjunction with each of the Kan primers (4 combinations of primers), the orientation of the Kanamycin cassette relative to the H.pylori sequence is determined. Positive clones are classified as either in the "A" orientation (the same direction of transcription is present for both the H. pylori gene and the Kanamycin resistance gene), or in the "B" orientation (the direction of transcription for the H.pylori gene is opposite to that of the Kanamycin resistance gene). Clones which share the same orientation (A or B) are pooled for subsequent experiments and independently transformed into H. pylori.

#### Transformation of Plasmid DNA into H. pylori cells

Two strains of *H. pylori* are used for transformation: ATCC <u>55679</u>, the clinical isolate which provided the DNA from which the *H. pylori* sequence database is obtained, and AH244, an isolate which had been passaged in, and has the ability to colonize the mouse stomach. Cells for transformation are grown at 37°C, 10% CO<sub>2</sub>, 100% humidity, either on Sheep-Blood agar plates or in Brucella Broth liquid. Cells are grown to exponential phase, and examined microscopically to determine that the cells are "healthy" (actively moving cells) and not contaminated. If grown on plates, cells are harvested by scraping cells from the plate with a sterile loop, suspended in 1 ml of

10

15

20

25

30

35

Brucella Broth, spun down (1 minute, top speed in eppendorf microfuge) and resuspended in 200 microliters Brucella Broth. If grown in Brucella Broth liquid, cells are centrifuged (15 minutes at 3000 rpm in a Beckman TJ6 centrifuge) and the cell pellet resuspended in 200 microliters of Brucella broth. An aliquot of cells is taken to determine the optical density at 600 nm, in order to calculate the concentration of cells. An aliquot (1 to 5 OD<sub>600</sub> units/25 microliter) of the resuspended cells is placed onto a prewarmed Sheep-Blood agar plate, and the plate is further incubated at 37°C, 6% CO<sub>2</sub>, 100% humidity for 4 hours. After this incubation, 10 microliters of plasmid DNA (100 micrograms per microliter) is spotted onto these cells. A positive control (plasmid DNA with the ribonuclease H gene disrupted by kanamycin resistance gene) and a negative control (no plasmid DNA) are done in parallel. The plates are returned to 37°C, 6% CO<sub>2</sub> for an additional 4 hours of incubation. Cells are then spread onto that plate using a swab wetted in Brucella broth, and grown for 20 hours at 37°C, 6% CO<sub>2</sub>. Cells are then transferred to a Sheep-Blood agar plate containing 25 micrograms/ml Kanamycin, and allowed to grow for 3 to 5 days at 37°C, 6% CO<sub>2</sub>, 100% humidity. If colonies appear, they are picked and regrown as patches on a fresh Sheep-Blood agar plate containing 25 micrograms/ml Kanamycin.

Three sets of PCR tests are done to verify that the colonies of transformants have arisen from homologous recombination at the proper chromosomal location. The template for PCR (DNA from the colony) is obtained by a rapid boiling DNA preparation method as follows. An aliquot of the colony (stab of the colony with a toothpick) is introduced into 100 microliters of 1% Triton X-100, 20 mM Tris, pH 8.5, and boiled for 6 minutes. An equal volume of phenol: chloroform (1:1) is added and vortexed. The mixture is microfuged for 5 minutes and the supernatant is used as DNA template for PCR with combinations of the following primers to verify homologous recombination at the proper chromosomal location.

TEST 1. PCR with cloning primers originally used to amplify the gene/ORF. A positive result of homologous recombination at the correct chromosomal location should show a single PCR product whose size is expected to be the size of the deleted gene/ORF but increased in size by the addition of a 1.4 kilobase Kanamycin cassette. A PCR product of just the size of the gene/ORF is proof that the gene had not been knocked out and that the transformant is not the result of homologous recombination at the correct chromosome location.

TEST 2. PCR with F3 (primer designed from sequences upstream of the gene/ORF and not present on the plasmid), and either primer Kan-1 or Kan-2 (primers designed from the ends of the kanamycin resistance gene), depending on whether the plasmid DNA used was of "A" or "B" orientation. Homologous recombination at the

10

15

20

25

30

35

correct chromosomal location will result in a single PCR product of the expected size (i.e., from the location of F3 to the insertion site of kanamycin resistance gene). No PCR product or PCR product(s) of incorrect size(s) will prove that the plasmid had not integrated at the correct site and that the gene had not been knocked out.

TEST 3. PCR with R3 (primer designed from sequences downstream of the gene/ORF and not present on the plasmid) and either primer Kan-1 or Kan-2, depending on whether the plasmid DNA used was of "A" or "B" orientation. Homologous recombination at the correct chromosomal location will result in a single PCR product of the expected size (i.e., from the insertion site of kanamycin resistance gene to the downstream location of R3). Again, no PCR product or PCR product(s) of incorrect size(s) will prove that the plasmid had not integrated at the correct site and that the gene had not been knocked out.

Transformants showing positive results for all three tests above indicate that the gene is not essential for survival *in vitro*.

A negative result in any of the three above tests for each transformant indicates that the gene had not been disrupted, and that the gene is essential for survival in vitro.

In the event that no colonies result from two independent transformations while the positive control with the disrupted ribonuclease H plasmid DNA produces transformants, the plasmid DNA is further analyzed by PCR on DNA from transformant populations prior to plating for colony formation. This will verify that the plasmid can enter the cells and undergo homologous recombination at the correct site. Briefly, plasmid DNA is incubated according to the transformation protocol described above. DNA is extracted from the *H. pylori* cells immediately after incubation with the plasmid DNAs and the DNA is used as template for the above TEST 2 and TEST 3. Positive results in TEST 2 and TEST 3 would verify that the plasmid DNA could enter the cells and undergo homologous recombination at the correct chromosomal location. If TEST 2 and TEST 3 are positive, then failure to obtain viable transformants indicates that the gene is essential, and cells suffering a disruption in that gene are incapable of colony formation

### VII. High-throughput drug screen assay

Cloning, expression and protein purification

Cloning, transformation, expression and purification of the *H. pylori* target gene and its protein product, e.g., an *H. pylori* enzyme, to be used in a high-throughput drug screen assay, is carried out essentially as described in Examples II and III above. Development and application of a screening assay for a particular *H. pylori* gene product, peptidyl-propyl *cis-trans* isomerase, is described below as a specific example.

#### Enzymatic Assay

10

20

25

30

The assay is essentially as described by Fisher (Fischer, G., et.al. (1984) *Biomed. Biochim. Acta* 43:1101-1111). The assay measures the *cis-trans* isomerization of the Ala-Pro bond in the test peptide N-succinyl-Ala-Ala-Pro-Phe-p-nitroanilide (Sigma # S-7388, lot # 84H5805). The assay is coupled with α-chymotrypsin, where the ability of the protease to cleave the test peptide occurs only when the Ala-Pro bond is in *trans*. The conversion of the test peptide to the trans isomer in the assay is followed at 390 nm on a Beckman Model DU-650 spectophotometer. The data are collected every second with an average scanning of time of 0.5 second. Assays are carried out in 35 mM Hepes, pH 8.0, in a final volume of 400 ul, with 10 μM α-chymotrypsin (type 1-5 from bovine Pancreas, Sigma # C-7762, lot 23H7020) and 10 nM PPIase. To initiate the reaction, 10 μl of the substrate (2 mM N-Succinyl-Ala-Ala-Pro-Phe-p-nitroanilide in DMSO) is added to 390 μl of reaction mixture at room temperature.

15 Enzymatic assay in crude bacterial extract.

A 50 ml culture of *Helicobacter pylori* (strain J99) in Brucella broth is harvested at mid-log phase (OD  $_{600~nm} \sim 1$ ) and resuspended in lysis buffer with the following protease inhibitors: 1 mM PMSF, and 10  $\mu$ g/ml of each of aprotinin, leupeptin, pepstatine, TLCK, TPCK, and soybean trypsin inhibitor. The suspension is subjected to 3 cycles of freeze-thaw (15 minutes at -70 °C, then 30 minutes at room temperature), followed by sonication (three 20 second bursts). The lysate is centrifuged (12,000 g x 30 minutes) and the supernatant is assayed for enzymatic activity as described above.

Many *H. pylori* enzymes can be expressed at high levels and in an active form in *E. coli*. Such high yields of purified proteins provide for the design of various high throughput drug screening assays.

#### **EQUIVALENTS**

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments and methods described herein. Such equivalents are intended to be encompassed by the scope of the following claims.

ACID SEQUENCES

### SEQUENCE LISTING

_	1) GENERAL INFORMATION:	
5	(1) 2007 702-	
	(i) APPLICANT: (A) NAME: Astra Aktie	ha1
	(B) STREET: S-151 85	botag
	(C) CITY: Sodertalje	
10	(D) STATE:	
	(E) COUNTRY: Sweden	•
	(F) POSTAL CODE (ZIP)	
15	(ii) TITLE OF INVENTION:	NUCLEIC ACID AND AMINO ACID SEQUENCE
13		RELATING TO HELICOBACTER PYLORI AND
		VACCINE COMPOSITIONS THEREOF
	(iii) NUMBER OF SEQUENCES: 20	08
20		
	(iv) COMPUTER READABLE FORM:	
	(A) MEDIUM TYPE:	
	(B) COMPUTER: (C) OPERATING SYSTEM:	
25	(D) SOFTWARE:	•
	(5, 5011111211	
	(v) CURRENT APPLICATION DATA	•
	(A) APPLICATION NUMBER	
30	(B) FILING DATE:	•
30	() PRIOR ARRITOR PAGE	
	(vi) PRIOR APPLICATION DATA: (A) APPLICATION NUMBER:	HC 00/230 150
	(B) FILING DATE: 28-OCT	-1996
	,	. 2330
35	(vii) PRIOR APPLICATION DATA:	
	(A) APPLICATION NUMBER:	US 08/759,739
	(B) FILING DATE: 06-DEC	C-1996
	(viii) PRIOR APPLICATION DATA:	
40	(A) APPLICATION NUMBER:	TIS 08/801 020
	(B) FILING DATE: 14-JUL	X-1997
	(ix) CORRESPONDENCE ADDRESS:	
45	(A) ADDRESSEE: LAHIVE &	COCKFIELD
43	(B) STREET: 28 State St	reet
	(C) CITY: Boston (D) STATE: Massachusett	
•	(E) COUNTRY: USA	S
	(F) ZIP: 02109-1875	
50		•
	(x) ATTORNEY/AGENT INFORMATI	
	(A) NAME: Mandragouras,	
	(B) REGISTRATION NUMBER	: 36,207
55	(C) REFERENCE/DOCKET NU	MBER: GTN-001CP10PC
رر	•	

```
(xi) TELECOMMUNICATION INFORMATION:
               (A) TELEPHONE: (617)227-7400
               (B) TELEFAX: (617)742-4214
     (2) INFORMATION FOR SEQ ID NO:1:
          (i) SEQUENCE CHARACTERISTICS:
              (A) LENGTH: 561 base pairs
               (B) TYPE: nucleic acid
10
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
15
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
20
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...561
25
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
     ATGATTAAAA GAATTGCTTG TATTTTAAGC TTGAGCGCGA GTTTAGCGTT AGCTGGCGAA
                                                                         60
     GTGAATGGGT TTTTCATGGG TGCGGGTTAT CAACAAGGTC GTTATGGCCC TTATAACAGC
                                                                         120
30 AATTACTCTG ATTGGCGTCA TGGCAATGAC CTTTATGGTT TGAATTTCAA ATTAGGTTTT
     GTAGGCTTTG CCAATAAATG GTTTGGGGCT AGGGTGTATG GCTTTTTAGA TTGGTTTAAC
     ACTTCAGGGA CTGAACACAC CAAAACCAAT TTGCTCACCT ATGGCGGCGG TGGCGATTTG
     ATTGTCAATC TCATTCCTTT GGATAAATTC GCTCTAGGTC TCATTGGTGG CGTTCAATTA
     GCCGGAAACA CTTGGATGTT CCCTTATGAT GTCAATCAAA CCAGATTCCA GTTCTTATGG
                                                                         420
     AATTTAGGCG GAAGAATGCG TGTTGGGGAT CGCAGTGCGT TTGAAGCGGG CGTGAAATTC
                                                                         480
     CCTATGGTTA ATCAGGGTAG CAAAGATGTA GGGCTTATCC GCTACTATTC TTGGTATGTG
                                                                         540
     GATTATGTCT TCACTTTCTA G
                                                                         561
     (2) INFORMATION FOR SEQ ID NO:2:
40
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 351 base pairs
             (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
45
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
50
        (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
              (A) ORGANISM: Helicobacter pylori
```

(ix) FEATURE:

	(A) NAME/KEY: misc_feature (B) LOCATION 1351	
	(2) 100:1101 1331	
. 5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:	
10	TTGATGCGCA TTATCATAAG GTTACTTTCA TTTAAAATGA ACGCTTTTT AAAACTCGCG CTCGCTTCTT TGATGGGGG GCTTTGGTAT GCTTTCAATG GCGAAGGCTC TGAGATTGTC GCTATAGGGA TTTTTGTGTT GATCTTGTTT GTTTTTTTTA TCCGCCCTGT GAGTTTCCAA GACCCAGAAA AACGAGAAGA ATACATAGAA CGGCTTAAAA AAAACCATGA GAGGAAAATG ATCTTACAAG ACAAGCAAAA AGAAGAGCAA ATGCGCCTCT ATCAAGCCAA AAAAGAGCGA GAGAGCAGGC AAAAACAAGA CCTTAAAGAA CAAATGAAAA AATACTCATA A	120 180 240 300
	CHARGAMA MATACICATA A	35:
15	(2) INFORMATION FOR SEQ ID NO:3:	٠
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1038 base pairs	
	(B) TYPE: nucleic acid (C) STRANDEDNESS: double	
20	(D) TOPOLOGY: circular	
	(2) Totologi. Circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
25	(iii) HYPOTHETICAL: NO	
23	(iv) ANTI-SENSE: NO	
	(IV) ANII-SENSE: NO	•
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
30		
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature (B) LOCATION 11038	
	(D) DOCKLOW I1030	
35	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:	-
	ATGGTTAAAC ACTATCTTTT CATGGCGGTT TCGCAGGTCT TTTTCTCCTT CTTTTTAGTG	60
	CTGTTTTTTA TCTCTTCCAT TGTGTTATTA ATCAGTATTG CAAGCGTAAC GCTCGTGATT	120
	AAAGTGAGCT TTTTGGATCT GGTGCAACTC TTTTTGTATT CCTTGCCAGG AACCATTTTT	180
40	TTTATTTTGC CGATCACTTT TTTTGCGGCT TGCGCTTTGG GGCTTTCAAG GCTTAGCTAT	240
	GACCATGAAT TGTTAGTGTT TTTCTCTTTA GGGGTTTCGC CTAAAAAAAT GACTAAAGCG	300
	TTTGTGCCTT TAAGTTTGTT AGTGAGCGCG ATTTTATTAG CGTTTTCGCT CATCTTAATC	360
	CCCACTTCTA AGAGCGCTTA TTACGGGTTT TTGCGTCAAA AAAAAGACAA GATTGACATT	420
45	AACATCAGAG CGGGTGAATT CGGGCAAAAA TTAGGCGATT GGCTCGTGTA TGTGGATAAG ACTGAAAACA ATTCCTATGA TAATTTGGTG CTTTTTTCTA ATAAAAGTCT CTCTCAAGAA	480
	AGCTTTATTT TGGCTCAAAA AGGCAATATC AACAATCAAA ACGGCGTGTT TGAATTGAAT	540 600
	TTGTATAACG GGCATGCGTA TTTCACTCAA GGCGATAAAA TGCGTAAGGT TGATTTTGAA	660
	GAATTGCATT TGCGCAACAA GCTCAAGTCT TTCAATTCTA ATGATGCGGC TTATTTGCAA	720
	GGCACGGATT ATTTGGGTTA TTGGAAAAAA GCCTTTGGTA AAAACGCTAA TAAAAATCAA	780
50	AAACGCCGTT TTTCTCAAGC GATCTTAGTT TCCTTGTTCC CTTTAGCGAG CGTGTTTTTA	840
	ATCCCCTTAT TTGGCATCGC CAACCCGCGA TTCAAAACGA ATTGGAGTTA TTTCTATGTC	900
	CTTGGAGCGG TTGGGGTTTA TTTTTTAATG GTGCATGTGA TTTCTACGGA TTTGTTTTTG	960
		1020
55	ATTTTAAAGC GTTATTAA	1038

WO 98/18323 PCT/US97/19575

- 91 -

```
(2) INFORMATION FOR SEQ ID NO:4:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 831 base pairs
5
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
10
        (iii) HYPOTHETICAL: NO
        (iv) ANTI-SENSE: NO
```

15 (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

(A) NAME/KEY: misc feature

20 (B) LOCATION 1...831

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

	ATGAAGAAAA	AAGCAAAAGT	CTTTTGGTGT	TGTTTTAAAA	TGATTCGTTG	GTTGTATTTG	60
25	GCGGTCTTTT	TTTTGTTGAG	CGTATCAGAC	GCTAAAGAAA	TCGCTATGCA	ACGATTTGAC	120
	AAACAAAACC	ATAAGATTTT	TGAAATCCTT	GCGGATAAAG	TGAGCGCCAA	AGACAATGTG	180
	ATAACCGCCT	CAGGGAATGC	GATCCTATTG	AATTATGACG	TGTATATTCT	AGCGGATAAG	240
	GTGCGTTATG	ACACCAAGAC	TAAAGAAGCG	TTATTAGAAG	GCAATATTAA	GGTTTATAGG	300
	GGCGAGGGCT	TGCTCGTTAA	AACCGATTAT	GTGAAATTGA	GTTTGAACGA	AAAATATGAG	360
30	ATCATTTTCC	CCTTTTATGT	CCAAGACAGC	GTGAGCGGGA	TTTGGGTGAG	CGCGGATATT	420
	GCTAGCGGGA	AGGATCAAAA	ATATAAGATT	AAAAACATGA	GCGCTTCAGG	GTGCAGCATT	480
	GACAACCCCA	TTTGGCATGT	CAATGCGACT	TCAGGCTCAT	TTAACATGCA	AAAATCGCAT	540
	TTGTCAATGT	GGAATCCTAA	${\bf GATTTATGTC}$	GGCGATATTC	CTGTATTGTA	TTTGCCCTAT	600
	ATTTTCATGT	CCACGAGCAA	TAAAAGAACT	ACCGGGTTTT	TATACCCTGA	GTTTGGCACT	660
35	TCCAACTTAG	ACGGCTTTAT	TTATTTGCAA	CCCTTTTATT	TAGCCCCCAA	AAACTCATGG	720
	GATATGACCT	TTACCCCACA	AATCCGTTAC	AAAAGGGGTT	TTGGCTTGAA	TTTTGAAGCG	780
	CGCTACATCA	ACTCTAAGAC	GCAGGTTTTT	ATTCAATGCG	CGCTATTTTA	G	831

(2) INFORMATION FOR SEQ ID NO:5:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 675 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
- 45 (D) TOPOLOGY: circular

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

50

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori

55

780

	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1675	
	(b) Bockflow 16/5	
5	(vi) SPOTENCE DESCRIPTION ON TO THE	
-	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:	
	ATCATURACAT TARRACCUMUT CARMARAS CO	
	ATGATTAGAT TAAAAGGTTT GAATAAAACT TTAAAAACAA GCTTATTAGC TGGGGTTTTA	60
	CTAGGTGCTA CTGCTCCCTT AATGGCAAAG CCTTTATTAA GCGATGAAGA CTTATTGAAA	120
10	CGAGTAAAAC TACACAATAT CAAAGAAGAT ACGCTGACTA GCTGTAATGC TAAGGTGGAC	180
10	GGCTCTCAAT ACTTGAATAG TGGTTGGAAT TTATCTAAAG AATTTCCGCA AGAATATAGA	240
	GAAAAGATTT TTGAATGCGT AGAAGAAGAA AAACATAAAC AAGCCCTTAA TTTAATCAAT	300
	AAAGAAGACA CTAAAGATAA AGAAGAACTT GCAAAAAAAA TCAAAGAAAT TAAAGAAAAA	360
	GCTAAAGTTT TAAGGCAAAA ATTTATGGCT TTTGAAATGA AAGAACACTC TAAAGAATTC	420
15	CCAAATAAAA AGCAACTTCA AACCATGCTT GAGAACGCTT TTGATAATGG AGCTGAAAGT	480
15	TITATIGATG ATTGGCACGA ACGCTTTGGG GGTATAAGTA GAGAGATAC TTATAAAGCA	540
-	CTTGGCATTA AAGAATATAG TGATGAAGGA AAGATATTGC CTTTGGCGAA AGAAGTTATA	600
	TTAGACAATA TAAAAAAGAT TTTGAAGAAA GCACTTATGA TACTAGACAA CCCTTATCTG	660
	CTATGGCTAG TATGA	675
20		
20	(2) INFORMATION FOR SEQ ID NO:6:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1290 base pairs	
~ =	(B) TYPE: nucleic acid	
25	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
30	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
35	(A) ORGANISM: Helicobacter pylori	
	•••	
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11290	
40		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:	
	ATGCCATACG CCTTAAGAAA AAGATTTTTC AAACGCCTTT TATTGTTTTT TTTAATTGTT	<b>C</b> 0
,	TGTATGATAA ATTTGCATGC CAAAAGCTAT CTGTTTTCTC CTTTGCCCCC AGCGCACCAG	60
45	CAAATCATTA AGACAGAGCC TTGCTCTTTG GAGTGCTTGA AAGACTTGAT GCTGCAAAAT	120
	CAAATCTTTT CTTTTGTATC CCAATACGAT GATAACAACC AAGATGAGAG CCTTAAAACT	180
	TATTACAAGG ACATCTTAAA CAAACTCAAC CCCGTATTCA TCGCTTCTCA AACTCCAGCT	240
	AAAGAAAGCT ATGAGCCTAA GATTGAATTA GCGATTTTAC TGCCTAAAAA GGTGGTGGGC	300
	CGTTATGCGA TTTTAGTGAT GAACACCCTT TTAGCGTATT TGAACACCAG AAACAACGAT	360
50	TTCAATATCC AAGTCTTTGA CAGCGATGAA GAAAGCCCTG AAAAATTAGA AGAAACCTAT	420
	AAAGAAATTG AAAAAGAAAA ATTCCCTTTT ATCATCGCTT TATTGACTAA AGAGGGCGTG	480
	GAAAATTTGC TCCAAAATAC GACTATCAAT ACCCCTT TATTGACTAA AGAGGGCGTG	540
	GAAAATTTGC TCCAAAATAC GACTATCAAT ACCCCTACTT ATGTGCCTAC GGTGAATAAA	600
	ACGCAATTAG AAAATCATAC CGAGCTTTCT TTAAGCGAGC GCTTGTATTT TGGGGGGATT	660
5	GATTATAAAG AGCAATTAGG CATGCTCGCA ACTTTCATTA GCCCTAATTC GCCCGTGATT	720

GAATACGATG ATGATGGCCT GATAGGTGAA CGCTTGAGGC AAATCACGGA GTCTTTAAAC

5	GTTGAAGTCA AACACCAAGA AAACATTTCT TACAAACAAG CGACCAGTTT TTCTAAAAAT TTTAGAAAAC ATGATGCGTT TTTTAAAAAT TCTACCTTAA TTTTGAACAC CCCTACCACT AAAAGCGGTC TGATCCTTC TCAAATAGGG CTTTTAGAGT ATAAGCCTCT TAAAATCCTT TCCACACAAA TCAATTTCAA CCCCTCTTTA CTCTTGCTCA CCCAGCCTAA AGACAGGAAA AATTTATTCA TTGTCAATGC CTTGCAAAAC AGCGATGAAA CGCTGATAGA ATACGCTTCC TTATTAGAGA GCGATTTAAG GCATGATTGG GTGAATTATT CCAGCGCGAT AGGGCTAGAG ATGTTTTTAA ACACGCTAGA TCCGCATTTT AAAAAGTCTT TTCAAGAGAG TTTGGAAGAC AATCAAGTCC GTTACCACAA TCAAATTTAT CAGGCTTTAG GGTATTCTTT TGAGCCGATA AAAAACGAAA GCGAAACAAA AAAAGAATAA	840 900 960 1020 1080 1140 1200 1260 1290
••	(2) INFORMATION FOR SEQ ID NO:7:	
15	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 1368 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
20	(ii) MOLECULE TYPE: DNA (genomic)	
20	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
25	<ul><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Helicobacter pylori</li></ul>	
	(ix) FEATURE:	
30	(A) NAME/KEY: misc_feature (B) LOCATION 11368	
30	(B) LOCATION 11368	
-	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:	
	GTGTTAAAAT TTCAAAAATT ACCCTTATTG TTTGTTTCCA TTCTTTATAA TCAAAGCCCT	60
35	TTATTGGCTT TTGATTATAA GTTTAGTGGG GTAGCGGAAT CTGTTTCTAA AGTGGGGTTT	120
	AACCATTCCA AACTCAATTC CAAAGAAGGG ATTTTCCCTA CAGCCACCTT TGTAACCGCC	180
	ACGATCAAGC TTCAAGTGGA TTCCAATCTG CTCCCTAAAA ACATTGAAAA ACACAGCTTA	240
	AAAATAGGCG TTGGGGGGAT TTTAGGAGCG CTCGCTTACG ATTCCACCAA AACGCTCATA	300
40	GACCAAGCCA CGCATCAAAT CTATGGCTCA GAACTTTTTT ACCTCATAGG GCGTTGGTGG	360
40	GGGTTTTTAG GCAACGCTCC TTGGAAAGAC TCCCTCATAG AATCTGACGC TCACACCCGT AATTATGTGC TGTATAATTC CTATCTGTTT TATTCTTATG GCGATAAATT CCACCTAAAA	420
	TTAGGGCGTT ATCTCTCTAA CATGGATTTT ATGAGTTCCT ACACACAGGG TTTTGAACTG	480 540
	GATTATAAAA TCAATTCTAA AATAGCGTTA AAATGGTTTA GCTCTTTTGG GAGGGCGTTG	600
•	GCTTTTGGGC AATGGATACG GGATTGGTAT GCCCCTATTG TAACTGAAGA TGGCAGAAAA	
45	GAAGTTTATG ATGGCATCCA TGCCGCGCAA CTCTATTTTT CTAGCAAGCA TGTTCAAGTC	
	ATGCCTTTTG CTTATTTTTC GCCTAAGATT TACGGAGCGC CCGGTGTTAA AATCCATATT	
	GATAGCAACC CGAAATTCAA AGGCTTAGGG TTAAGGGCTC AAACCACTAT TAATGTGATT	840
•	TTCCCTGTTT ATGCTAAAGA TTTATACGAT GTGTATTGGC GTAACTCTAA GATTGGCGAG	
	TGGGGCGCAT CGCTTTTGAT CCACCAACGC TTTGACTACA ACGAATTTAA CTTTGGCTTT	960
50		1020
		1080
		1140
		1200
Ė E		1260
55	CACAACGGCT ATAGATTAGA CTATCTCACC GGCCCTTTCA ACAAAGCCTT TAAGGCTGAC	1320

1368

GCACAAGATA GGAGTAACCT TATGGTTAGC ATGAAATTCT TTTTTTAA

#### (2) INFORMATION FOR SEQ ID NO:8: 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 849 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular 10 (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO 15 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori 20 (ix) FEATURE: (A) NAME/KEY: misc feature (B) LOCATION 1...849 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8: 25 ATGGGGTGTT CGTTTATCTT TAAAAAAGTT AGGGTTTATT CTAAAATGTT GGTTGCTTTG GGGCTTTCAA GCGTGTTGAT CGGTTGCGCG ATGAATCCAA GCGCTGAGAC AAAAAAACCA 120 AATGACGCCA AAAACCAACA ACCAGTTCAA ACTCATGAAA GAATGACAAC AAGTTCTGAA 180 CATGTTACGC CACTAGATTT TAATTACCCG GTGCATATTG TTCAAGCCCC ACAAAACCAT 240 CATGTTGTAG GTATTTTAAT GCCACGCATT CAAGTGAGCG ATAATCTAAA ACCCTATATT 300 GATAAGTTTC AAGACGCTTT AATTAATCAA ATCCAAACTA TTTTTGAAAA AAGAGGCTAT 360 CAAGTGTTGC GTTTTCAAGA TGAAAAAGCT TTGAATGTGC AAGATAAGAA AAAGATTTTT 420 TCCGTTTTGG ATTTGAAAGG GTGGGTAGGA ATCTTAGAAG ATTTGAAAAT GAATTTAAAA 480 GATCCCAATA GTCCCAATTT AGACACGCTA GTGGATCAAA GCTCAGGCTC TGTATGGTTT 540 AATTTTTATG AACCAGAAAG CAATCGTGTC GTCCATGATT TTGCTGTAGA AGTAGGAACT TTTCAGGCAA TAACATACAC ATACACCTCT ACTAATAACG CTTCAGGAGG GTTTAATTCT TCAAAAAGCG TTATCCATGA AAATTTGGAT AAGAATAGAG AAGACGCGAT ACACAAGATT TTAAACAGAA TGTATGCGGT TGTCATGAAA AAAGCTGTAA CAGAACTTAC AAAAGAAAAT 780 ATCGCCAAAT ACAGAGACGC TATTGATAGA ATGAAAGGCT TTAAAAGTTC TATGCCTCAA 840 40 AAAAAGTAG 849 (2) INFORMATION FOR SEQ ID NO:9: (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 843 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular 50 (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

```
(A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
 5
              (A) NAME/KEY: misc feature
              (B) LOCATION 1...843
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:
    ATGAAACTGA GAGCAAGTGT TTTAATCGGT GTGGCAATTC TGTGCTTAAT TTTAAGTGCG
     TGCAGTAACT ATGCGAAAAA AGTGGTGAAA CAAAAGAACC ATGTTTATAC GCCTGTGTAT
    AATGAACTGA TAGAGAAGTA TAGTGAGATC CCCTTAAATG ACAAACTCAA AGACACACCA
     TTCATGGTGC AAGTGAAGTT GCCAAATTAC AAGGACTATT TGTTGGATAA TAAACAAGTT
    GTACTAACTT TCAAACTTGT TCACCATTCT AAAAAGATTA CGCTCATAGG CGATGCCAAT
    AAGATCCTCC AATACAAGAA TTACTTCCAA GCTAACGGGG CAAGATCTGA CATTGATTTT
    TACTTGCAAC CCACTTTGAA TCAAAAGGGT GTGGTGATGA TAGCGAGTAA CTACAATGAT
    AATCCCAACA ACAAAGAAAA ACCACAGACC TTTGATGTGT TGCAAGGAAG TCAGCCAATG
    CTAGGAGCTA ACACAAAAA CTTGCATGGC TATGATGTGA GTGGAGCAAA CAACAAGCAA
    GTGATCAATG AAGTGGCAAG AGAAAAAGCT CAGCTAGAAA AAATCAATCA GTATTACAAG
20
    ACTCTCTTGC AAGACAAGGA ACAAGAATAT ACCACTAGGA AAAATAACCA ACGAGAAATT
                                                                      660
    TTAGAAACAT TGAGTAATCG TGCAGGTTAT CAAATGAGGC AGAATGTGAT TAGTTCTGAG
                                                                      720
    ATTTTTAAGA ATGGCAACTT GAACATGCAA GCCAAAGAAG AAGAAGTTAG GGAGAAGCTA
                                                                      780
    840
                                                                      843
25
     (2) INFORMATION FOR SEQ ID NO:10:
         (i) SEQUENCE CHARACTERISTICS:
              (A) LENGTH: 1179 base pairs
30
              (B) TYPE: nucleic acid
              (C) STRANDEDNESS: double
              (D) TOPOLOGY: circular
        (ii) MOLECULE TYPE: DNA (genomic)
35
       (iii) HYPOTHETICAL: NO
       (iv) ANTI-SENSE: NO
40
        (vi) ORIGINAL SOURCE:
              (A) ORGANISM: Helicobacter pylori
        (ix) FEATURE:
              (A) NAME/KEY: misc feature
45
              (B) LOCATION 1...1179
        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:
    ATGAGAAAAC TATTCATCCC ACTTTTATTA TTCAGCGCTT TAGAAGCGAA CGAGAAAAAC
    GGCTTTTTCA TAGAAGCCGG CTTTGAAACT GGGCTATTAG AAGGCACACA AACGCAAGAA 120
    AAAAGACACA CCACCACAAA AAACACTTAC GCAACTTACA ATTATTTACC CACAGACACG
    ATTTTAAAAA GAGCGGCTAA TTTATTCACC AATGCCGAAG CGATTTCAAA ATTAAAATTC 240
    TCATCTTTAT CCCCTGTTAG AGTGTTGTAT ATGTATAATG GTCAATTAAC TATAGAAAAC
                                                                     300
    TTCTTGCCTT ATAATTTAAA TAATGTTAAG CTTAGTTTTA CAGACGCTCA AGGCAATGTG
                                                                     360
55 ATCGATCTAG GCGTGATAGA GACTATCCCC AAACACTCTA AGATTGTTTT GCCCGGAGAG
```

	GCATTTGATA GTCTAAAAAT TGACCCCTAT ACTTTATTTC TTCCAAAAAT TGAAGCCACT	480
	AGCACTTCTA TTTCTGACGC TAACACGCAG AGGGTGTTTG AAACGCTCAA TAAGATTAAG	540
	ACAAATTTGG TCGTAAATTA TAGGAATGAA AACAAATTTA AAGATCACGA AAATCATTGG	600
	GAAGCCTTTA CCCCACAAAC CGCAGAAGAA TTCACTAATT TAATGTTGAA CATGATCGCT	660
. 5	GTTTTAGACT CCCAATCTTG GGGCGATGCG ATCTTAAACG CTCCTTTTGA GTTCACTAAC	720
-	AGCCCAACAG ATTGCGATAA TGATCCTTCA AAATGCGTAA ATCCTGGGAC AAACGGGCTT	780
	GTCAATTCTA AAGTCGATCA AAAATATGTG TTAAACAAAC AAGACATTGT CAATAAATTT	840
	AAAAACAAAG CGGATCTTGA TGTAATTGTT TTAAAGGATT CAGGGGTTGT AGGGCTTGGG	900
	AGTGATATTA CCCCTAGCAA CAATGATGAT GGCAAGCATT ATGGCCAGTT AGGGGTAGTA	960
10	GCTTCTGCTT TAGATCCTAA AAAACTCTTT GGCGATAACC TTAAGACTAT CAATTTAGAG	1020
	GATTTAAGAA CCATCTTGCA TGAATTCAGC CACACTAAAG GCTATGGGCA TAACGGGAAT	1080
	ATGACCTATC AAAGAGTGCC GGTAACGAAA GATGGTCAAG TGGAAAAGGA TAGTAATGGC	1140
	AAGCCAAAAG ATTCTGATGG CCTCCCCTAT AATGTGTGT	1179
15	(2) INFORMATION FOR SEQ ID NO:11:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 813 base pairs	
	(B) TYPE: nucleic acid	
20	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	, , , , , , , , , , , , , , , , , , , ,	
	(ii) MOLECULE TYPE: DNA (genomic)	
25	(iii) HYPOTHETICAL: NO	
	· · · · · · · · · · · · · · · · · · ·	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
30	(A) ORGANISM: Helicobacter pylori	
	(iii) oiliana manadada piracra	
	(ix) FEATURE:	
	(A) NAME/KEY: misc feature	
	(B) LOCATION 1813	
35		
	(xi) SEQUENCE DESCRIPTION: SEO ID NO:11:	
	ATGAAAAGT TTGTAGCTTT AGGGCTTCTA TCCGCGGTTT TAAGCTCTTC GTTGTTAGCC	60
	GAAGGTGATG GTGTTTATAT AGGGACTAAT TATCAGCTTG GACAAGCCCG TTTGAATAGC	120
40	AATATTTATA ATACAGGGGA TTGCACAGGG AGTGTTGTAG GTTGCCCCCC AGGTCTTACC	180
	GCTAATAAGC ATAATCCAGG AGGCACCAAT ATCAATTGGC ACTCCAAATA CGCTAATGGG	240
	GCTTTGAATG GTTTTGGGTT GAATGTGGGT TATAAGAAAT TCTTCCAATT CAAGTCGCTA	300
	GATATGACAA GCAAGTGGTT TGGTTTTAGA GTGTATGGGC TTTTTGATTA CGGGCATGCC	360
	GATTTAGGTA AACAAGTTTA TGCACCTAAT AAAATCCAGT TGGATATGGT CTCTTGGGGT	
45	GTGGGGAGCG ATTTGTTAGC TGATATTATT GATAAAGACA ACGCTTCTTT TGGTATTTTT	
	GGTGGGGTCG CTATCGGCGG TAACACTTGG AAAAGCTCTG CAGCAAACTA TTGGAAAGAG	540
	CAAATCATTG AAGCCAAAGG TCCTGATGTT TGTACCCCTA CTTATTGTAA CCCTAATGCC	600
	CCTTATAGCA CCAACACTTC AACCGTCGCT TTTCAAGTGT GGTTGAATTT TGGGGTGAGA	660
	GCCAATATCT ACAAGCATAA TGGCGTGGAA TTTGGCGTGA GAGTGCCGCT ACTCATCAAT	
50	AAATTTTTGA GCGCGGGTCC TAACGCTACT AACCTTTATT ACCATTTGAA ACGGGATTAT	
•	TCGCTTTATT TGGGGTATAA CTACACTTTT TAA	813
	·································	
	(2) INFORMATION FOR SEQ ID NO:12:	

55 (i) SEQUENCE CHARACTERISTICS:

_	<ul><li>(A) LENGTH: 423 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li><li>(D) TOPOLOGY: circular</li></ul>	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
10	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1423</pre>	
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:	. •
20	ATGCATCCTA TAATGTTTGC CTATATCGCT AACGCGCTCG CTCAAGCTAG AAAGATCAAC GGAACACTTT GCATGGCGTT TCAAAAAATA TCTCAAGTCA AAGAATTAGG CATTGATAAA GCAAAGAGTT TGATAGGCAA CCTTTCTCAA GTGATTATCT ACCCCACAAA AGATACTGAT GAATTAATAG AATGTGGCGT CCCATTAAGC GATAGTGAAA TCAATTTCTT ACACAACACG	120 180 240
25	GACATGAGAG CCAGACAAGT GCTAGTAAAA AATATCGTTA CAAACGCTTC AGCTTTATT GAAATTGATT TAAAAAAGAT TTGCAAGAAC TACTTTATAT TCTTGATAGC AATGCTGGTA ATAGAAAAAT CCTCAATGAT CTTAAAAAAG CAAACCAAGA AACTTATAAG GAAGAGTATT TAA	300 360 420 421
30	(2) INFORMATION FOR SEQ ID NO:13:	
35	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 771 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
	(ii) MOLECULE TYPE: DNA (genomic)	
40	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
45	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1771</pre>	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:	
55	ATGTTGGGGA GCGTCAAAAA AGCGGTTTTT AGGGTTTTGT GTTTGGGGGC GTTGTGTTTA TGCGGGGGGT TAATGGCAGA GCAAGATCCT AAAGAGCTTA TATTTTCAGG TATAACTATT TACACGGATA AAAATTTCAC TAGAGCTAAG AAATATTTTG AAAAAGCTTG CAAATCAAAC	6: 12: 18:

	GATGCTGATG GCTGTGCAAT CTTAAGAGAG GTTTATTCTA GTGGTAAAGC CATAGCGAGA	240
	GAAAACGCAA GAGAGAGCAT TGAAAAAGCT CTTGAACACA CCGCTACTGC TAAAGTTTGT	300
	AAATTAAACG ATGCTGAAAA ATGCAAGGAC TTAGCAGAGT TTTATTTTAA TGTAAACGAT	360
	CTTAAAAATG CTTTAGAATA TTACTCTAAA TCTTGTAAGT TAAATAATGT TGAAGGGTGT	420
5	ATGCTGTCAG CAACTTTTTA TAACGATATG ATAAAGGGTT TGAAAAAAGA TAAAAAAGAT	480
	CTAGAATATT ATTCTAAAGC TTGCGAGTTA AATAACGGTG GAGGGTGTTC TAAATTAGGA	540
	GGGGATTATT TTTTTGGTGA AGGCGTAACA AAAGATTTCA AAAAAGCTTT TGAATATTCT	600
	GCCAAAGCTT GTGAGTTGAA CGATGCTAAA GGGTGTTACG CTCTAGCAGC GTTTTATAAT	660
	GAGGGTAAAG GCGTGGCAAA GGATGAAAAG CAAACGACAG AAAACCTTGA AAAGAGTTGC	720
10	AAGCTAGGAT TAAAAGAAGC ATGCGATATT CTCAAAGAAC AAAAACAATA A	771
	(2) INFORMATION FOR SEQ ID NO:14:	
. ~	(i) SEQUENCE CHARACTERISTICS:	
15	(A) LENGTH: 729 base pairs	•
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
•	(D) TOPOLOGY: circular	
20	(ii) MOLECULE TYPE: DNA (genomic)	
20	(II) MODECOLE TIPE: DNA (GENOMIC)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
25		
	(vi) ORIGINAL SOURCE:	•
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
30	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1729	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:	
35	ATGAAAAAT TTTTTTCTCA ATCTTTGTTA GCTCTTATTA TCTCTATGAA TGCGGTATCT	50
,,,	GGCATGGATG GTAATGGCGT TTTTTTAGGG GCGGGTTATT TGCAAGGACA GGCGCAAATG	60
	CATGCGGATA TTAATTCTCA AAAACAAGCC ACCAACGCTA CGATCAAAGG CTTTGACGCG	120
	CTCTTGGGGT ATCAATTTT CTTTGAAAAA CACTTTGGCT TACGCCTTTA TGGGTTTTTT	180
	GACTACGCTC ATGCCAATTC TATTAAGCTT AAAAACCCTA ACTATAATAG CGAAGCGGCG	240
40	CAAGTGGCTA GTCAAATTCT TGGGAAACAA GAAATCAATC GTTTAACAAA CATTGCCGAT	300
	CCCAGAACTT TTGAGCCGAA CATGCTCACT TATGGGGGGG CTATGGACGT GATGGTTAAT	360
	GTCATCAATA ACGGCATCAT GAGTTTGGGG GCTTTTGGCG GGATACAATT GGCCGGCAAT	420
	TCATGGCTTA TGGCGACACC GAGCTTTGAG GGCATTTTAG TGGAACAAGC CCTTGTGAGC	480
	AAGAAAGCCA CTTCTTTCCA ATTTTTATTC AATGTGGGGG CTCGCTTAAG GATCTTAAAA	540
15	CATTCTAGCA TTGAAGCGGG CGTGAAATTC CCCATGCTAA AGAAAAACCC CTACATCACT	600
	GCAAAAAATT TGGATATAGG GTTTAGGCGC GTGTATTCGT GGTATGTGAA TTACGTGTTC	660
	ACTITICIAG	720
	MOLLI GIFTO	729
	(2) INFORMATION FOR SEQ ID NO:15:	
50		
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 804 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
55	(D) TOPOLOGY: circular	

	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
5	(111) MITOIMITUME. NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
10	(A) ORGANISM: Helicobacter pylori	-
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature (B) LOCATION 1804	
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:	
	ATGAACTACC CTAATCTACC TAACAGCGCT TTAGAGATAA GCGAACAGCC AGAAGTGAAA	60
	GAAATCACTA ACGAGCTTTT AAAGCAATTA CAAAACGCTT TAAGGAGCAA CGCGCATTTT	120
20	AGCGAGCAAG TGGAATTAAG CCTTAAATGC ATCGTTAGGA TTTTAGAAGT GCTTTTGAGT TTGGATTTTT TTAAGAATGC GAATGAGATT GATAGCAGTT TAAGAAATTC CATTGAGTGG	180
20	CTGACTAACG CCGGCGAGAG CTTGAAATTA AAAATGAAAG AATACGAGCG CTTTTTTAGC	240 300
	GAGTTTAATA CGAGCATGCA TGCCAACGAG CAGGAAGTAA CCAATACCTT AAACGCTAAC	360
	GCCGAGAACA TTAAAAGCGA AATTAAAAAG CTAGAAAATC AATTGATAGA AACCACGACA	420
	AGACTTTTAA CGAGCTATCA AATCTTTTTA AACCAAGCCA GAGATAACGC TAACAACCAA	480
25	ATCACAAAAA ACAAAACCCA AAGCCTTGAA GCGATTACAC AAGCTAAAAA CAACGCTAAT	540
٠	AATGAAATAA GCAACAATCA AACGCAAGCG ATAACTAATA TCACCGAAGC GAAAACGAAC	600
	GCTAATAATG AAATAAGCAA CAATCAAACG CAAGCGATAA CTAACATTAA CGAAGCCAAA	660
	GAAAGCGCTA CAACGCAAAT AAACGCCAAT AAGCAAGAAG CAATAAATAA CATCACGCAA	720
30	GAAAAAACCC AAGCCACAAG CGAGATCACC GAAGCGAAAA AGACCGATCA TTATCAAAAC ATTGATTTTT TTGAGTTTGA ATAA	780 804
,,,	ALLONITIE LIGHTING AIRS	004
	(2) INFORMATION FOR SEQ ID NO:16:	
	(i) SEQUENCE CHARACTERISTICS:	
35	(A) LENGTH: 1632 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
40	(ii) MOLECULE TYPE: DNA (genomic)	
•	(11) Holder III Star (genomic)	
	(iii) HYPOTHETICAL: NO	
15	(iv) ANTI-SENSE: NO	
-	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
50	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11632	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:	
55	GTGATAGAGA CCATCCCCAA ACACTCTAAG ATTGTTTTAC CCGGGGAGGC GTTTGATAGT	60
-	The coordinated	00

	· · · · · · · · · · · · · · · · · · ·	
	TTAAAAGAGG CGTTTGATAA AATTGACCCC TATACTTTCT TTTTTCCAAA ATTTGAAGCC	120
	ACTAGCACTT CTATTTCTGA TACTAACACG CAGAGGGTGT TTGAAACGCT CAATAACATT	
	AAAACAAATC TTATAATGAA ATATAGTAAT GAAAATCCAA ACAATTTCAA CACTTGTCCT	180
	TACAATAATA ATGGTAATAC AAAAAATGAT TGTTGGCAAA ATTTCACCCC ACAAACCGCA	240
5	GAAGAATTCA CCAATTTAAT GTTGAACATG ATCGCTGTCT TAGACTCCCA ATCTTGGGGC	300
	GATGCGATCT TAAACGCTCC TTTTGAATTC ACTAACAGCT CAACAGATTG CGATAGCGAT	360
,	CCTTCAAAAT GCGTAAATCC CGGAGTAAAT GGGCGTGTTG ATACTAAAGT CGATCAACAA	420
	TATATACTCA ACAAACAAGG TATTATTAAT AATTTTAGAA AAAAAATAGA AATTGATGCG	480
	GTTGTTTTAA AAAATTCAGG GGTTGTAGGG TTAGCCAATG GATATGGCAA TGATGGTGAA	540
10	TATGGCACAT TAGGGGTACA AGGGTAMGGT TTAGGCAATG GATATGGCAA TGATGGTGAA	600
••	TATGGCACAT TAGGGGTAGA AGCCTATGCT TTAGATCCTA AAAAACTCTT TGGCAACGAC	660
	CTTAAGACTA TCAATTTAGA AGATTTAAGA ACCATCTTGC ATGAATTCAG CCACACTAAA	720
	GGCTATGGGC ATAACGGGAA TATGACCTAT CAAAGAGTGC CGGTAACGAA AGATGGTCAA	780
	GTGGAAAAGG ATAGTAATGG CAAGCCAAAA GATTCTGATG GCCTCCCCTA TAATGTGTGT	840
15	TCGCTTTATG GGGGATCCAA TCAGCCCGCT TTCCCTAGCA ACTACCCTAA TTCCATCTAT	900
.13	CACAATTGTG CGGATGTCCC GGCTGGCTTT TTAGGGGTAA CAGCAGCGGT TTGGCAGCAG	960
	CTCATCAATC AAAACGCCTT GCCGATCAAC TACGCTAACT TGGGGAGTCA AACAAACTAC	1020
	AACCTAAACG CTAGTTTAAA CACGCAAGAT TTAGCCAATT CCATGCTCAG CACCATCCAA	1080
	AAAACCTTTG TAACTTCTAG CGTTACCAAC CACCATTTTT CAAACGCATC GCAAAGTTTT	1140
20	AGAAGCCCTA TTTTAGGGGT TAACGCTAAA ATAGGCTATC AAAACTACTT TAATGATTTC	1200
20	ATAGGGTTGG CTTATTATGG CATCATCAAA TACAATTACG CTAAAGCTGT TAATCAAAA	1260
	GTCCAGCAAT TGAGCTATGG TGGGGGGATA GATTTGTTAT TGGATTTCAT CACCACTTAC	1320
	TCCAATAAA ATAGCCCTAC AGGCATTCAA ACCAAAAGGA ATTTTTCTTC ATCTTTTGGT	1380
	ATCTTTGGGG GGTTAAGGGG CTTGTATAAC AGCTATTATG TGTTGAACAA AGTCAAAGGA	1440
	AGCGGCAATT TAGATGTGGC TACCGGGTTG AACTACCGCT ATAAGCATTC TAAATATTCT	1500
25	GTAGGGATTA GCATCCCTTT AATCCAAAGA AAAGCTAGCG TCGTTTCTAG CGGTGGCGAT	1560
	TATACGAACT CTTTTCTTTT CAATCAACCC COTACCC COTACCC	1620
	GGTGGGTCTT TT	1632
	(2) INFORMATION FOR SEQ ID NO:17:	
30		
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1071 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
3.5	(D) TOPOLOGY: circular	
	, and a second s	
	(ii) MOLECULE TYPE: DNA (genomic)	
	y described the state of the st	
	(iii) HYPOTHETICAL: NO	
40		
	(iv) ANTI-SENSE: NO	
	(11) IIII DENDE. NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
45	(A) ORGANISM: HellCobacter pylori	
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11071	
50	(vi) SPOHENCE DESCRIPTION	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:	
50		
50	TTGATGAAAA GCATTTTGCT CTTTATGATT TTTGTAGTTT GTCAGTTAGA AGGCAAAAA	60
50	TTGATGAAAA GCATTTTGCT CTTTATGATT TTTGTAGTTT GTCAGTTAGA AGGCAAAAAA TTTTCACAAG ATAATTTTAA GGTGGATTAT AACTACTATT TGCGCAAACA GGATTTGCAC	60 120
	TTGATGAAAA GCATTTTGCT CTTTATGATT TTTGTAGTTT GTCAGTTAGA AGGCAAAAAA TTTTCACAAG ATAATTTTAA GGTGGATTAT AACTACTATT TGCGCAAACA GGATTTGCAC ATCATTAAAA CGCAAAACGA TTTGTCCAAT GCCTGGTATC TCCCTCCACA AAAAGCCCCCC	-
50	TTGATGAAAA GCATTTTGCT CTTTATGATT TTTGTAGTTT GTCAGTTAGA AGGCAAAAAA TTTTCACAAG ATAATTTTAA GGTGGATTAT AACTACTATT TGCGCAAACA GGATTTGCAC	120

960

	ACTTATTTTT TGCCTTTTTA TCATAGTTTC ACCCCCATTT TTCAATGGTA CCACCCTAAT	300
	ATCAACCCCT ACCAACGCAA TGAGTTTAAG TTCCAAATCA GTTTTAGAGT GCCTGTATTT	360
	AGGCATATTC TTTGGACTAA AGGCACGCTT TATCTGGCTT ATACCCAAAC TAACTGGTTT	420
	CAAATTTATA ATGACCCTCA ATCCGCCCCC ATGCGAATGA TCAATTTCAT GCCTGAACTC	480
5	ATCTATGTTT ATCCTATTAA TTTTAAACCT TTTGGGGGTA AAATAGGGAA TTTTTCTGAA	540
-	ATTTGGATAG GTTGGCAGCA CATTTCTAAT GGTGTGGGGG GTGCGCAATG TTACCAGCCT	600
	TTTAATAAAG AAGGTAATCC TGAAAACCAG TTTCCAGGAC AACCTGTAAT CGTTAAAGAT	660
	TATAACGGGC AAAAAGATGT GCGCTGGGGG GGGTGTCKTT CGGTGARCSC GGGCAACSCC	720
	CTGTGTTTCG TTTTGGTGTG GGAAAAGGGA GGCCTAAAAA TCATGGTCGC TTATTGGCCC	780
10	TATGTCCCTT ATGATCAATC CAACCCTCAA TTGATTGATT ACATGGGGTA TGGTAACGCT	840
,	AAAATTGATT ACAGGAGAGG GCGCCACCAT TTTGAATTGC AACTTTATGA TATTTTCACG	900
-	CAATACTGGC GTTATGATCG CTGGCATGGA GCTTTCCGCT TAGGCTATAC CTACCGCATT	
	AACCCTTTTG TGGGGATTTA TGCGCAGTGG TTTAACGGCT ATGGCGATGG CTTGTATGAA	960
	TACGATGTTT TTTCCAATCG TATAGGGGTA GGAATACGCT TGAACCCTTA A	
15	*** COMMITTEE THE CONTROL OF THE CON	1071
	(2) INFORMATION FOR SEQ ID NO:18:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 2028 base pairs	
20	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	,	
	(ii) MOLECULE TYPE: DNA (genomic)	
25		
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
20		
30	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
25	(A) NAME/KEY: misc_feature	
35	(B) LOCATION 12028	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:	
	MINISTERNAL COMPANY OF THE COMPANY O	
40	TTGTCTAAAG GTTTGAGTAT CGGTAATAAA ATCATATTGT GCGTGGCGTT GATTGTGATC	60
40	GTGTGCGTGA GCATTTTAGG GGTGTCCTTA AACAGCAGGG TGAAAGAGAT TTTAAAAGAA	120
	AGCGCTCTGC ATTCAATGCA AGATAGTTTG CATTTCAAGG TTAAGGAAGT GCAAAGTGTT	180
	TTGGAAAACA CTTATACGAG CATGGGCATT GTCAAAGAAA TGCTCCCTGA AGACACCAAA	240
	AGAGAAATCA AAATCCAGTT GTTAAAAAAC TTCATTTTAG CCAATTCGCA TGTCGCTGGG	300
45	GTGAGCATGT TTTTTAAAGA CAGAGAGGAT TTGAGATTGA CGCTTTTACG AGATAACGAT	360
43	ACGATCAAGT TGATGGAAAA CCCGTCATTA GGGAGTAACC CTTTAGCGCA AAAAGCGATG	420
	AAAAATAAAG AAATTTCTAA AAGCTTGCCT TATTACAGGA AAATGCCTAA CGGGGCGGAA	480
	GTTTATGGCG TGGATATTCT TTTACCACTA TTCAAGGAAA ACACGCAAGA AGTGGTGGGG	540
	GTTCTGATGA TTTTCTTTTC CATTGACAGC TTCAGTAATG AAATCACTAA AAACAGGAGC	600
50	GATTTATTT TAATTGGCGT TAAAGGTAAA GTGCTTTTGA GCGCGAATAA AAGCTTGCAA	660
50	GACAAATCCA TCACCGAAAT TTATAAAAGC GTGCCTAAAG CCACTAATGA AGTGATGGCT	720
	ATTTTAGAAA ATGGCTCTAA AGCGACTTTA GAATACTTGG ATCCCTTTAG CCATAAGGAG	780
	AATTTTTTAG CCGTTGAAAC CTTTAAAATG CTAGGCAAAA CAGAAAGTAA AGACAATCTT	840
	AATTGGATGA TCGCTTTGAT CATTGAAAAA GACAAGGTCT ATGAGCAAGT GGGATCGGTG	900
	CGTTTTGTGG TGGTTGCAGC GAGTGCTATC ATGGTGTTAC CCTTTA ATGATT AGGGTTGT CTT	~ ~ ~

CGTTTTGTGG TGGTTGCAGC GAGTGCTATC ATGGTGTTAG CCTTAATCAT AGCGATCACT

CTTTTAATGC GAGCGATCGT GAGCAATCGT TTGGAAGTCG TTTCTAGCAC CTTGTCTCAT 1020

	·	
	TTCTTTAAAT TATTGAACAA TCAAGCCCAT TCTAGCGACA TTAAATTGGT TGAAGCGCGA	1080
	TCTAATGACG AATTAGGGCG CATGCAAACA GCGATCAATA AAAATATCTT GCAAACCCAA	1140
	AAAACCATGC AAGAAGACAC CCAAGGGGGG GAAGAGAGAGAGAGA	1200
	AAAGCGGGGA ATTTTGCGGT GCGCATCACG GCTGAACCCG CAAGCCCTGA TTTGAAAGAA	1200
- 5	TTGAGAGACG CCCTAAATCC CATCATCCAT TATTER TO THE TOTAL TO THE TOTAL TO THE TOTAL TO THE TOTAL TOTA	
-	CCAACCATTT TCAAATCTT TCAAACCTAT TCAAACCTAT	1320
	ALCCCTTCCC CTACCCCCA ATTCCCTTACA TCTGCCTTCG ATTTTAGAGG GCGGATCCAA	1380
	AACGCTTCGG GTAGGGTGGA ATTGGTTACT AACGCTTTAG GGCAAGAAAT CCAAAAAATG	1440
	CTAGAAACTT CGTCTAATTT TGCCAAAGAT CTAGCGAACG ATAGCGCGAA TTTAAAAGAA	1500
10	TGCGTGCAAA ATTTAGAAAA GGCTTCAAAC TCCCAACACA AAAGCCTGAT GGAAACTTCC	1560
10	AAAACGATAG AAAATATCAC CACTTCCATT CAAGGCGTGA GCTCTCAAAG TGAAGCCATG	1620
	ATTGAACAAG GGAAAGACAT TAAAAGCATT GTAGAAATCA TTAGAGATAT TGCCGATCAA	1680
	ACGAATCTAT TAGCCCTAAA CGCTGCTATT GAAGCCGCAC GAGCCGGCGA GCATGGCAGA	1740
	GGCTTTGCGG TGGTGGCTGA TGAGGTGAGG AAGCTCGCTG AAAGGACGCA AAAATCCCTC	1800
	AGTGAGATTG AAGCCAATAT TAATATTCTC GTTCAAAGCA TTTCAGACAC GAGCGAAAGC	
15	ATTAAAAACC AGGTTAAAGA AGTAGAAGAG ATCAACGCTT CTATTGAAGC CTTAAGATCG	1860
	GTTACTGAGG GCAATCTAAA AATCGCTAGC GATTCTTTAG AAATCAGTCA AGAAATTGAC	1920
	AAAGTCTCTA ACGATATTTT AGAAGATGTG AATAAAAAGC AGTTTTAA	
	ACAMANTI AGAMANTOTO AATAAAAGC AGTTTTAA	2028
	(2) INFORMATION FOR SEQ ID NO:19:	
20	(2) INFORMATION FOR SEQ ID NO:19:	
20	(i) CROWNING CONTRACTOR	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 816 base pairs	
	(B) TYPE: nucleic acid	
25	(C) STRANDEDNESS: double	
23	(D) TOPOLOGY: circular	
		,
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
30	(iii) HYPOTHETICAL: NO	
30	(iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO	
30		
30		
	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	
30 35	(iv) ANTI-SENSE: NO	
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
	<pre>(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:</pre>	
	<pre>(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE:</pre>	
35	<pre>(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:</pre>	
	<pre>(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:</pre>	
35	<pre>(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:</pre>	
35	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	60
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	60 120
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120 180
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120 180 240
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori  (ix) FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 1816  (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:  ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCCTTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATGCA CCTTGTTGGT TTGGCCCAATA TCCATGTGGA GCCCTTTAAGA	120 180 240 300
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120 180 240 300 360
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120 180 240 300 360 420
35 40	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori  (ix) FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 1816  (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:  ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCCTTTATAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATGCA CCTTGTTGGT TTGGCCAATA ACCCTTGTGGA GCCTTTAAGA TTTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAACA AGGCCTTATTC	120 180 240 300 360 420 480
35 40 45	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori  (ix) FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 1816  (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:  ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCATA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT AATTTGGACA GAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG CCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATGACA AGGCCTTATC GCTCCTAAAGA ACCCCTAAAGA ACCCTTAACA AGGCCTTATC GCTCCTCAAAGA ACCCCAAAGCAA TCTATACGCT ACGGGGTTTG ATATTGTCAA AAACCCTTAACC	120 180 240 300 360 420 480 540
35 40 45	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120 180 240 300 360 420 480 540 600
35 40 45	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120 180 240 300 360 420 480 540 600 660
35 40 45	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori  (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816  (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:  ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGTTT AATTTGAGA GAAAAATCAC CCTTGTTGGT TTGGCCAATA TCCATGTGGA GCCTTTAAGA TTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAAA AAGGCTCAGT GATTGCTGTG CCCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAAACA AGGCCTTATC ACGACGTTTG ACCCCAAAGAAAAC CCCAAGCAA TCTATACGCT TTGATTTTAC TCCATAAACA AGGCCTTATC ACGACGTTTG ATATTGTCAA AAACCTTAACA AGGCCTTAC ACGAGGTTTG ATATTGTCAA AAACCTTAC ACGAGGTTTG ATATTGTCAA AAACCCTTAC ACGAGGTTTG ATATTGTCAA AAACCTTTAC GGATGTGGAT TTATTGCCTTG CAAGCAAAAC TCAACCCCT AGAAGCTCG CTAATCTTCC GGAGGATAA TCCACCGAGCA TTATTTTCA GGATGTGGAT TTATTGCCTTG CAAGCAAAAC TCAACCCCTA TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTGCCTTG CAAGCAAAAC TCACCGGGAGA TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTTTCA CAAGCAAAAC TCACCGGGATAA TCACCCGAGCA TTATTTTCA CAAGCAAAAC TCACCGGGAGA TTATTGCCTTG CAAGCAAAAC TCACCGGAGT TTATTTTCA CAAGCAAAAC TCACCGGGAGA TTATTGCCTTG CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCGCGTTA TGCTAATCTT CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAACA TCACCCCTTA TGCTAAACCT CTAAACCTTT CCATGAGCATAA TCCACCAAGAAAC TCACCCCAAACA TCACCCCTAAACA TCACCCCTAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCTAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAAAAC TCACCCCAAACA TAATTGCCTTG CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAAAAC TCACCCCAAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAAAAC TCACCCCAAAAAC TCACCCAAAAAC TCACCCCAAAAAC TCACCCAAAAAC TCACCCCAAAAAC TCACCCCAAAAAC TCACCCAAAAAC TCACCCAAAAAC TCACCCAAAAAC TCACCCAAAAAC TCACCCAAAA	120 180 240 300 360 420 480 540 600 660 720
35 40 45 50	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:	120 180 240 300 360 420 480 540 600 660
35 40 45	(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori  (ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1816  (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:  ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT TTAGACGCCA AACACCACAA AGAAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA GAGAAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGTTT AATTTGAGA GAAAAATCAC CCTTGTTGGT TTGGCCAATA TCCATGTGGA GCCTTTAAGA TTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAAA AAGGCTCAGT GATTGCTGTG CCCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAAACA AGGCCTTATC ACGACGTTTG ACCCCAAAGAAAAC CCCAAGCAA TCTATACGCT TTGATTTTAC TCCATAAACA AGGCCTTATC ACGACGTTTG ATATTGTCAA AAACCTTAACA AGGCCTTAC ACGAGGTTTG ATATTGTCAA AAACCTTAC ACGAGGTTTG ATATTGTCAA AAACCCTTAC ACGAGGTTTG ATATTGTCAA AAACCTTTAC GGATGTGGAT TTATTGCCTTG CAAGCAAAAC TCAACCCCT AGAAGCTCG CTAATCTTCC GGAGGATAA TCCACCGAGCA TTATTTTCA GGATGTGGAT TTATTGCCTTG CAAGCAAAAC TCAACCCCTA TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTGCCTTG CAAGCAAAAC TCACCGGGAGA TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTGCCTTG CAAGCAAAAC TCACCGGGGAT TTATTTTCA CAAGCAAAAC TCACCGGGATAA TCACCCGAGCA TTATTTTCA CAAGCAAAAC TCACCGGGAGA TTATTGCCTTG CAAGCAAAAC TCACCGGAGT TTATTTTCA CAAGCAAAAC TCACCGGGAGA TTATTGCCTTG CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCGCGTTA TGCTAATCTT CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAACA TCACCCCTTA TGCTAAACCT CTAAACCTTT CCATGAGCATAA TCCACCAAGAAAC TCACCCCAAACA TCACCCCTAAACA TCACCCCTAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCTAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAAAAC TCACCCCAAACA TAATTGCCTTG CAAGCAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAAAAC TCACCCCAAAAAC TCACCCGAGC CTTATTTTCA CAAGCAAAAC TCACCCCAAAAAC TCACCCCAAAAAC TCACCCAAAAAC TCACCCCAAAAAC TCACCCAAAAAC TCACCCCAAAAAC TCACCCCAAAAAC TCACCCAAAAAC TCACCCAAAAAC TCACCCAAAAAC TCACCCAAAAAC TCACCCAAAA	120 180 240 300 360 420 480 540 600 660 720

• 6	(2) INFORMATION FOR SEQ ID NO:20:	
5	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 486 base pairs  (B) TYPE: nucleic acid	
٠.	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
10	(ii) MOLECULE TYPE: DNA (genomic)	
-	(iii) HYPOTHETICAL: NO	
15	(iv) ANTI-SENSE: NO	
	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	ï
20	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1486</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:	
25	ATGTTTTTA AAACTTATCA AAAATTACTG GGCGCGAGCT GTTTGGCGCT GTATTTAGTG GGCTGTGGGA ATGGTGGTGG CGGTGAATCG CCGGTTGAGA TGATTGCAAA TAGCGAGGGT ACGTTTCAAA TCGACTCCAA AGCAGATAGC ATTACTATTC AAGGCGTGAA GCTTAATAGA GGTAATTGTG CTGTCAATTT TGTTCCAGTA AGTGAGACGT TTCAAATGG TGTTTTAAGT	60 120 180 240
30	CAAGTTACTC CAATCTCTAT ACAGGATTTT AAAGATATGG CAAGCACTTA TAAGATATTT GATCAAAAGA AAGGGTTGGC AAACATAGCA AATAAAATTT CTCAATTAGA GCAAAAGGGT GTGATGATGG AACCTCAAAC CCTTAATTTT GGAGAAAGGTT TAAAAGGCAT TTCTCAAGGG TGCAATATTA TAGAGGCAGA AATACAAACC GACAAAGGCG CTTGGACTTT TAACTTTGAT AAATAA	300 360 420 480 486
35	(2) INFORMATION FOR SEQ ID NO:21:	
40	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 1014 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li><li>(D) TOPOLOGY: circular</li></ul>	
	(ii) MOLECULE TYPE: DNA (genomic)	
45	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
<b>50</b> .	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
55	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 11014	

55

420

480

540

600

660

720

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

	2 15 NO.571:	
	ATGATTAGAT TAAAAGGTTT GAATAAAACT TTAAAAAACAA GCTTATTAGC TGGGGTTTTA	60
:	CTAGGTGCTA CTGCTCCCTT AATGGCAAAG CCTTTATTAA GCGATGAAGA CTTATTCAAA	
5	CGAGTAAAAC TACACAATAT CAAAGAAGAT ACGCTGACTA GCTGTAATGC TAAGGTGGAC	120
	GGCTCTCAAT ACTTGAATAG TGGTTGGAAT TTATCTAAAG AATTTCCGCA AGAATATAGA	180
	GAAAAGATTT TTGAATGCGT AGAAGAAGAA AAACATAAAC AAGCCCTTAA TTTAATCAAT	240
	AAAGAAGACA CTGAAGATAA AGAAGAACTT GCAAAAAAAA TCAAAGAAAA TAAAGAAAAA	300
	GCTAAAGTTT TAAGGCAAAA ATTTATGGCT TTTGAAATGA AAGAACACTC TAAAGAATTC	360
10	CCAAATAAAA AGCAACTTCA AACCATGCTT GAGAACGCTT TTGATAATGG AGCTGAAAGT	420
	TTTATTGATG ATTGGCACGA ACGCTTTGGG GGTATAAGTA GAGAGAATAC TTATAAAGCA	480
	CTTGGCATTA AAGAATATAG TGATGAAGGA AAGATATTAG CCTTTGGCGA AAGAAGTTAT	540
	ATTAGACAAT ATAAAAAGA TTTTGAAGAA AGCACTTATG ATACTAGACA AACCTTATCT	600
	GCTATGGCTA ATATGAGTGG CGAAAACGAT TATAAAATTA CTTGGTTAAA ACCCAAATAT	660
-15	CAGCTCCATA GTTCAAATAA TATTAAACCC TTAATGTCAA ACACAGAGTT GTTAAATATG	720
	ATAGAGCTAA CCAATATCAA AAAAGAATAT GTTATGGCT GTAATATGGA AATAGATGGT	780
	TCTAAATATC CCATTCATAA AGATTGGGGA TTTTTTGGTA AGGCAAAAGT CCCAGAAACT	840
	TGGAGAAATA AGATTTGGGA ATGTATTAAG AATAAAGTAA AGTCCTATGA CAACACTACC	900
	GCTGAAATAG GAATAGTTTG GAAAAAAAAT ACTTATTCTA TCTCTCATCA CTAA	960
20	ACTIATICIA TOTOTOATOA CTAA	1014
	(2) INFORMATION FOR SEQ ID NO:22:	
	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 1251 base pairs	
25	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(ii) was now a series	
30	(ii) MOLECULE TYPE: DNA (genomic)	
50	/iii Indominatas	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(17) MILL OBIGE. NO	
35	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
**	(ix) FEATURE:	
40	(A) NAME/KEY: misc_feature	
70	(B) LOCATION 11251	
	(vi) SPOJENCE DECONTRACTOR OF THE	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:	
-	ATGAAAAAT TACTTTTAG CATGGTTTTAA GGTTGTTAA	
45	ATGAAAAAT TAGTTTTTAG CATGCTTTTA TGTTGTAAAA GCGTGTTTGC AGAGGGGGAA	60
	ACTCCTTTGA TTGTCAATGA CCCAGAAACC CATGTAAGTC AAGCCACTAT CATAGGCAAA	120
	ATGGTAGATA GTATCAAAAG ATACGAAGAG ATTATTTCTA AGGCTCAAGC TCAAGTCAAT	180
	CAGTTACAAA AAGTCAATAA CATGATAAAT ACGACTAATT CTTTGATTAG TAGTAGTGCT	240
	ATCACTTTAG CCAATCCTAT GCAAGTTTTA CAAAACGCTC AGTATCAAAT AGAGAGCATT	300
50	AGATACAACT ATGAGAATTT AAAGCAAAGC ATAGAAAATT GGAACGCACA AAATTTGTTA	360
-0	AGAAACAAAT ACTTACAGCA ACAATGCCCT TGGCTTAATG TCAATGCTCT TACTACAAT	420

AGAAACAAAT ACTTACAGCA ACAATGCCCT TGGCTTAATG TCAATGCTCT TACTAACAAT

AAGATTGTCA ATCTTAAAGA TCTCAATAAC CTAATCACCA AAAATGGCGA ACAAACCCAA

ACCGCAAGAG ATGTGCAAAA TCTCATTCAG TCCATTAGTG GCAGTGGCTA TGGAAACATG

CAATCACTTG CTGGGGAATT GAGTGGTAGA GCGTGGGGGG AAATGTTGTG TAAAATGGTA

AACGATAGTA ATTATGAAAG CGAGCAAGCT CTTTTAGCAA CAGGCAATAA CCCAGAAGAG

CAAAAACGAA GATTTTTGCT TAGAGTAAAG AAAAAGGTTA ATGATAATAA GCAGTTAAAA

5	GATAAACTTG ACCCATTTCT AAAAAGACTT GATGTCCTAC AAACTGAGTT TGGTGTAACT GACCCTACAG CTAACCATAA TAAGCAAGGG ATACATTATT GCACAGAAAA TAAAGAGACA GGTAAATGCG ACCCTATTAA AAATGTATTT AGGACAACTC GCTTAGATAA CGAATTAGAA CAAGAAATCC AAACGCTCAC ACTTGATTTA ATCAAAGCCT CCAATAAAGA CGCTCAAAGC CAAGCCTACG CAAATTTCAA TCAAAGGATT AAATTACTTA CTCTAAAATA TTTAAAAGAA ATTACCAATC AAATGCTCTT TTTAAATCAA ACAATGGCAA TGCAAAGCGA GATTATGACA GATGATTATT TTAGGCAAAA TAATGATGGC TTTGGGGAAA AAGAAAACCA TATAGACAAA CAATTAACGC AAAAAAGAAT AAACGAAAGA GAAAGAGCTA GAATATACTT TCAAAACCCT AATGTTAAAT TTGACCAATT TGGCTTTCCC ATTTTTAGTA TATGGGATTA A	940 900 960 1020 1080
	(2) INFORMATION FOR SEQ ID NO:23:	
15	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 1131 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
•	(ii) MOLECULE TYPE: DNA (genomic)	
20	(iii) HYPOTHETICAL: NO	-
	(iv) ANTI-SENSE: NO	
25	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
30	(ix) FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 11131	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:	
35	GTGAATAAGT GGATTAAAGG GGCGGTTGTT TTTGTAGGGG GTTTTGCAAC GATTACAACC TTTTCTTTAA TCTACCACCA AAAGCCAAAA GCCCCCCTAA ATAACCAGCC TAGCCTTTTG AATGACGATG AGGTGAAATA CCCCTTACAA GACTACACTT TCACTCAAAA CCCACAGCCA ACTAACACGG AAAGCTCCAA AGACGCTACC ATCAAAGCCT TACAAGAACA GCTCAAAGCC	60 120 180 240
	GCTTTAAAAG CCCTAAACTC CAAAGAAATG AATTATTCCA AAGAAGAGAC TTTTACTAGC	300
40	CCTCCCATGG ATCCAAAAAC AACCCCCCCT AAAAAAGACT TTTCTCCAAA ACAATTAGAT	360
40	TTACTGGCCT CTCGCATCAC CCCTTTCAAG CAAAGCCCTA AAAATTACGA AGAAAACCTG ATTTTCCCTG TGGATAACCC TAATGGCATT GATAGTTTCA CTAACCTTAA AGAAAAAGAC	420
	ATCGCCACTA ATGAAAACAA GCTTTTACGC ACCATTACAG CTGACAAAAT GATACCCGCT	480 540
• .	TTTTTGATTA CGCCCATTTC TAGCCAGATC GCTGGTAAAG TGATTGCGCA AGTGGAGAGC	600
	GATATTTTTG CAAGCATGGG CAAAGCCGTC TTAATCCCCA AAGGCTCTAA AGTCATAGGC	660
45	TATTACAGCA ACAATAACAA AATGGGCGAA TACCGCTTGG ATATTGTATG GAGTCGAATC	720
•	ATCACTCCCC ATGGCATTAA TATCATGCTC ACTAACGCTA AAGGGGCGGA CATTAAAGGC	780
	TATAACGGCT TAGTGGGGGA ATTGATTGAA AGGAATTTCC AACGCTATGG CGTGCCGTTA	840
	CTGCTTTCTA CGCTCACTAA CGGCCTATTG ATTGGGATCA CTTCGGCTTT AAACAACAGA GGCAATAAAG AAGAGGTGAC TAATTTCTTT GGGGATTATC TTTTATTGCA ATTGATGAGG	900
50	CAAAGCGGCA TGGGGATCAA TCAAGTGGTC AATCAAATTT TAAGAGACAA GAGCAAGATC	360
	GCCCCCATTG TGGTGATTAG AGAGGGGAGT AGGGTCTTCA TTTCGCCCAA TACTGACATC	1020
	TTCTTCCCTA TACCCAGAGA GAATGAAGTC ATCGCTGAGT TTTTGAAGTG A	1131
	(2) INFORMATION FOR SEC ID NO.24.	

```
(i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 2751 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
 5
              (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
       (iii) HYPOTHETICAL: NO
10
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
          (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...2751
20
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:
     GTGGATTTGA GGATCCAATC TAAAGAAGTC AGTCATAATT TAAAGGAATT ATCAAAAACG
                                                                         60
     CTAATCAGCT ATCCTTTTGA AAAACATGTA GAAGCTTTAG GGGAACAATG CAGTAACTTC
                                                                        120
     GTTTCTATTC CCATTAACAA TGACGACTAT TCAAATATTT GCACTTTTGT GAGTGATTTT
                                                                        180
     ATAAATCTTA TAGCTTCTTA CAATTTATTA GAATCATTTT TAGATTTTA TAAAGATAAA
     TTAAAATTGA GCGAGCTTGT AACTGAATAT GCCAACGTAA CCAATAATCT GCTTTTCAAA 300
     AAATTAATCA AACATTTAAG CGGCAACAAT CAATTGGTTA AAAATTTTTA TCAGTGTATA
    AGAGAAATTA TAAAATACAA CGCCCCTAAT AAAGAATACA AACCCAATCA ATTTTTTATA
                                                                        420
     ATAGGGAAAG GCAAACAAAA ACAATTAGCA AAAATTTATT CTCATTTAAA AGAACTTAGT
                                                                        480
30
    GCAAGTGAAA TTAAACCACA AGATATGGAA GACATCTTAA AAAAGCTAGA GGAATTAGAT
    AAAATTTTTA AAACTACCGA CTTTACAAAA TTCACACCAA AAACTGAAAT TAAGGATATT
                                                                        600
    ATTAAAGAAA TAGACGAAAA ATACCCTATC AATGAAAATT TTAAACGGCA ATTTAATGAG
                                                                        660
    TTTGAATCAA ATATTGAAAA ACATGATGAA ATAAAAAAGG ATTTTGAGCG AAACAAAGAG
    TCGCTGATCC GAGAAATTGA AAATCACTGC AAAAATGAAT GCAATAGCGA AGAAGAGCCG
    GAGTATAAGA TTAATGATCT GCTCAAAAAT ATCCAACAAA TATGCAAAAA TTATATAGAA
                                                                        840
    AGTCATGCCG TTAATGATGT GTCTAAAGAT ATTAAATCCA TGATGTGTCA GTTTTATTTG
                                                                        900
    AAACAGATAG ATTTATTAGT CAATTCAGAA ATTGTGCGAT ACAGATACAG CAATCTTTTT
    GAACCAATAC AAAGATCTTT ATGGGAGAGT ATAAAAATTT TAGATAATGA AAGTGGCATT 1020
    TATTTGTTCC CTAAAAATAT TGGTGAAATC AAGGATAAAT TTGAAGCAAA CAAGGAAAAA
    TTCAAACAAA GCAAAAATGT TTCTGAGTTC GCAGAATATT GCCGAGAGTG TAACCCCTAT
    ACAGCGTTTA ACTTTCATCT AAATATAAAT AATGGTTTAT CTCATCAATT TGAAAAATTC
    GTGCCAATCA TGAAAGAATA CAAAGAGCCA AAAATCACAG ATAATGACCT TGAAGCCATA 1260
    TCAACCAAAG AGACTGGTCT TGCTAGCCAA TTATCTGGGC ACTGGTTTTT TCAGCTTTCG 1320
    TTATTTAATA AAACAAACTT TAATCCTAAT AAAATTTGGA TTCCTTTAGA GTTCAATAAA 1380
    AGATCAAAAA TAAAGTTTGA TAAAGATTTA GAAATCTATT TTGATAGTCA TGAATCGTTC 1440
    AATATCTCTA AAAAATACTT GCAAGAAATA GATCAAGAAT CACTAAAAAA GATCAAACAA 1500
    TCAAAAGATT TTTTTCAAT TCAAAAAATA GAGAGTAAGC ATGATAATAA CGATATACTG 1560
    CAACTTGAAT TTTTTGAGAA TGATACAAGT TTTCTTTTTG CTAAAGGAAG TTTTGCAGAA 1620
    ATTTTAGAAT ACAACATGCA ATTAAAAATA GATTCTTTAA TTACAAAAGA ATTTAATAAG 1680
    CTTTTAGCGA TCGTTCAAGA TAGTCCCCAA GATAGTTACC AATTAAAAAT TCGTGTCCGA 1740
    CATAACAATA AGCTTCCTAG AGAGAAATAT ACGGAACATG AAATAAAACT TGAAGTTTAT 1800
    GATTGCAGAA AATCCCACGA TCACAATGAG CCAATCATCT TAAGCCAGCA AAGCACCGGC 1860
    TTCCAATGGG CGTTTAATTT CATGTTTGGC TTTCTTTATA ATGTGGGATC ACATTTTAGT
    TTTAACCATA ATATTATCTA TGTCATGGAC GAGCCAGCCA CTCATTTGAG CGTGCCAGCC
    AGAAAGGAGT TTAGGAAATT TTTAAAAGAA TACGCTCATA AAAATCATGT TACTTTTGTT 2040
```

5	TTAGCCACCC ATGACCCCTT TTTAGTGGAT ACGGATCATT TAGATGAAAT AAGGATTGTG GAAAAGGAAA CAGAAGGCTC TGTAATTAAG AATCACTTTA ACTATCCCT AAATAATGCA AGCAAAGACT CCGACGCTTT GGACAAAATC AAACGCTCTT TAGGAGTGGG CCAGCATGTT TTTCATAACC CCCAAAAACA CCGAATCATT TTTGTAGAAG GCATCACGGA TTATTGTTAT TTGAGCGCTT TTAAATTGTA TTTGCGTTAC AAAGAATACA AGGACAACCC CATTCCTTTC ACTTTCTTAC CCATTTCAGG GCTTAAAAAC GATTCAAACG ATATGAAAGA AACCATTGAA AAACTTTGCG AGTTAGACAA TCACCCTATT GTTTTGACAG ACGATGACAG AAAATGCGTT TTTAACCAAC AAGCAACGAG CGAACGATTT AAAAGAGCTA ATGAAGAAAT GCATGATCCC ATCACCATCC TACAACTCTC AGACTGCGAT AGGCATTTCA AACAAATTGA AGATTGTTTC AGCGCAAACG ATAGAAACAA ATACGCTAAA AATAAGCAAA TGGAATTGAG CATGGCTTTT AAAACAAGGC TTTTGTATGG CGGAGAAGAT GCGATAGAAA AACAAACAAA AAGAAATTTT TTAAAAATTAT TCAAATGGAT TGCATGGGCT ACAAACTTGA TCAAAAACTA A	-
15	(2) INFORMATION FOR SEQ ID NO:25:  (i) SEQUENCE CHARACTERISTICS:	
20	<ul><li>(A) LENGTH: 531 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li><li>(D) TOPOLOGY: circular</li></ul>	
20	*	
	(ii) MOLECULE TYPE: DNA (genomic)	
25	(iii) HYPOTHETICAL: NO	
<i>23</i>	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
30	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	•
	(A) NAME/KEY: misc_feature (B) LOCATION 1531	
35	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:	
•	ATGACTGCAA TGATGCGTTA TTTTCACATC TATGCGACCA CTTTTTTCTT CCCTTTTGGCG	60
• •	CTTCTTTTTG CGGTTAGTGG GCTTTCATTG CTCTTTAAAG CGCGCCAAGA CACTGGCGCT AAGATCAAAG AATGGGTTTT AGAAAAAATCC TTAAAAAAAAG AAGAACGATT GGACTTTTTA	120 180
40	AAAGGCTTTA TAAAAGAAAA CCATATCGCT ATGCCTAAAA AGATAGAGCC TAGAGAGTAT	240
	AGGGGAGCGT TAGTCATTGG CACGCCTTTG TATGAAATCA ACCTTGAAAC TAAAGGCACT CAAACGAAAA TCAAGACCAT TGAAAGGGGC TTTTTAGGCG CGCTCATCAT GCTGCATAAG	300 360
	GCTAAGGTGG GCATCGTGTT TCAGGCGCTT TTAGGGATTT TTTGCGTGTT TTTATTGTTG	420
45	TTTTACTTGA GCGCGTTTTT AATGGTGGCT TTTAAAGACA CTAAACGCAT GTTTATAAGC	480
	GTTTTAATAG GGAGCGTGGT GTTCTTTGGA GCGATCTATT GGTCTTTGTA G	531
	(2) INFORMATION FOR SEQ ID NO:26:	
50	(i) SEQUENCE CHARACTERISTICS:	
50	(A) LENGTH: 669 base pairs (B) TYPE: nucleic acid	•
	(C) STRANDEDNESS: double	
,	(D) TOPOLOGY: circular	
55	(ii) MOLECULE TYPE: DNA (genomic)	

	(iii) HYPOTHETICAL: NO	•
5	(iv) ANTI-SENSE: NO	
,	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	•
	(ix) FEATURE:	
10	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1669	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:	
15	ATTCTTTTA A A A COCCUMUNA A A TO	
	ATGTTTAAAA ACGCTTTAAA TATACAAGAT TTTTCATTTA AAAATCATAC TAGTACAGCC ATTATTGGCA CAAATGGTGC TGGAAAATCA ACGCTTATCA ACACTATTCT AGGCATTAGA	6
7	ICAGACTATA ATTITIAAAGC ACAAAACAAT AATATTCCAT ACCACCACAA TCTTATAGCA	120
	CAACGCAAGC AATTGGGAGT TGTCTCTAAC CTATTCAACT ACCCACCTGG ATTAAACGCA	240
20	AACGACCTTT TTAAATTCTA TCAATTTTTT CACAAAAACT GCACTCTAGA TTTGTTTTGAA	300
20	AAAAATCTTT TAAATAAAAC CTACGAACAC CTAAGCGACG GACAAAAACA GCGCTTAAAA ATTGACTTAG CTCTTAGCCA TCACCCACAA TTAGTTATTA TGGATGAACC AGAAACCAGT	.366
	TAGAGCAAA ACGCTCTTAT AAGACTATCA AATCTCATAA GCTTGCGCAA CACCCAACAA	420
	CITACAAGTA TCATCGCCAC TCATGATCCT ATTGTCTTAG ATAGTTCCCA ATCCCTATTCC	480 540
25	CICCITAAGA ATGGCAACAT TGCTCAATAC AAACCTTTAA ATTCTATATT AAAATCTCTA	600
	GCTAAAACTT TTAACTTTAA AGAAAAACCA ACCACAAAAG ACTTATTAGC GTTACTAAAG GATATTTAA	660
	4.7	669
	(2) INFORMATION FOR SEQ ID NO:27:	
30	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1221 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
35		
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
40	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
45		
40	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature</pre>	
	(B) LOCATION 11221	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:	
	ATGTATGCGG CTCATCCTAT TAAACCCATA AAAGCCCCTA AACTCAAATC TCAATTTTTA	<b>.</b> -
	AGGCGIGIGI TIGIGGGCGC GTCCATTAGG CGCTGGAATG ACCAAGCATG CCCTTTTCCAA	60 120
	IIIGIGGAAT TAGACAAGCA AGCCCATAAA GCGATGATTG CGTATCTGCT CGCTAAACAT	180
55	TTAAAAGATA GGGGTAAAGA TTTAGATTTA GATCTTTTAA TCAAATATTT TTGCTTTGAG TTTTTTGGAGC GCTTGGTTTT AACCGATATT AAACCCCCTA TTTTTTTACGC CCTCCAACAA	240
	AACCCCCTA TTTTTACCC CCTCCAACAA	300

900

1.		
	ACGCATAGTA AAGAGTTAGC TTCCTATGTT GCGCAAAGTT TGCAAGATGA AATCAGTGCG	360
	TATTTTCTT TAGAGGAACT CAAAGAGTAT TTAAGCCACA GGCCTCAAAT TTTAGAAACT	420
. :	CAAATTTTAG AGAGCGCGCA TTTTTATGCG TCTAAGTGGG AGTTTGATAT TATCTATCAT	
	TTTAACCCCA ACATGTATGG CGTGAAAGAG ATTAAAGATA AAATTGACAA GCAACTCCAC	540
5	AATAACGATC ATTTGTTTGA AGGGCTTTTT GGGGAAAAAG AAGATTTGAA AAAATTGGTG	600
	AGCATGTTTG GGCAGTTGCG TTTCCAAAAG CGCTGGAGCC AAACCCCAAG AGTGCCACAA	660
	ACCAGTGTTC TAGGGCATAC TTTATGCGTG GCGATTATGG GGTATTTATT GAGTTTTGAC	720
	TTGAAAGCTT GTAAAAGCAT GCGGATCAAT CATTTTTTGG GCGGGCTTTT CCATGATTTA	720
	CCCGAAATTT TAACCCGAGA CATTATCACG CCCATCAAAC AAAGCGTTGC AGGGCTTGAT	840
10	CATTGCATTA AAGAGATTGA AAAAAAGGAA ATGCAAAACA AAGTCTATTC CTTTGTGTCT	900
	TTGGGCGTTC AAGAAGATTT GAAATATTTC ACCGAAAACG AGTTTAAAAA CCGCTACAAA	960
	GACAAGTCTC ATCAAATCGT TTTCACTAAA GACGCTGAAG AATTATTCAC GCTTTATAAT	1020
	AGCGATGAAT ATCTTGGGGT TTGCGGGGAG CTTTTGAAGG TGTGCGATCA TTTGAGCGCG	1020
•	TTTTTAGAAG CCCAAATCTC TCTTTCTCAT GGCATTTCTA GCTACGATTT AATCCAAGGA	1140
15	GCTAAAAACC TTTTAGAATT GCGATCCCAA ACGGAACTGC TTGATTTGGA TTTAGGGAAA	
	TTGTTTAGAG ATTTTAAGTA A	1200
		1221
	(2) INFORMATION FOR SEQ ID NO:28:	
	(2) Intoldination for Big 15 No.25.	
20	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1008 base pairs	•
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
25	(b) Torobodi. Circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(11) MODECODE TIPE. DAK (GENOMIC)	
	(iii) HYPOTHETICAL: NO	
•	(III) MIOIMIICAD. NO	
30	(iv) ANTI-SENSE: NO	
50	(IV) ANII DENOE. NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ii) ondizini nerreobacter pyrorr	
35	(ix) FEATURE:	
	(A) NAME/KEY: misc feature	
	(B) LOCATION 11008	
	(b) LOCATION 11000	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:	
40	(111) DIRECTION DIDENTIFICATION ON TO NO.20:	
	GTGTTGTGGG TGCTATATTT TTTAACCAGT TTATTTATTT GCTCTTTGAT TGTTTTGTGG	
	TCTAAAAAAT CCATGCTCTT TGTGGATAAC GCTAATAAAA TCCAAGGCTT CCATCATGCA	60 3130
:	AGAACCCCAC GAGCCGGGGG GCTTGGGATC TTTCTTTCTT TTGCGTTGGC TTGTTATCTT	120
	GAACCTTTTG AGATGCCTTT TAAGGGGCCT TTTGTTTTCT TAGGGCTATC GCTAGTGTTT	180
45	TTGAGCGGTT TTTTAGAAGA CATTAACCTT TCATTAAGCC CCAAAATACG CCTTATTTTG	240
73	CANCETETAC COUNCETTE CATCAUTICA MONAGOCOM TO THE CONTEST OF THE CATCAUTICA MONAGOCOM TO THE CONTEST OF THE CATCAUTICA MONAGOCOM TO THE CONTEST OF THE CATCAUTICA MONAGOCOM TO THE CATCAUTICA MONAGOCOM	300
	CAAGCTGTAG GGGTCGTTTG CATCATTTCA TCAACGCCTT TAGTGGTGAG CGATTTTTCG	360
	CCCCTTTTTA GCTTGCCTTA TTTCATCGCT TTTTTATTCG CTATTTTTAT GCTGGTGGGT	420
	ATCAGTAACG CTATTAATAT CATTGACGGG TTTAACGGGC TTGCATCTGG GATTTGCGCG	480
50	ATCGCGCTTT TAGTCATTCA TTATATAGAC CCTAGCAGTT TGTCTTGTTT GCTCGCTTAC	540
50	ATGGTGCTTG GGTTTATGGT GTTAAATTTC CCTTCAGGAA AGATTTTTTT AGGCGATGGG	600
	GGGGCGTATT TTTTGGGTTT GGTGTGCGGG ATTTCTCTCT TGCATTTGAG TTTGGAGCAA	660
	AAAATCAGCG TGTTTTTTGG GCTCAATTTA ATGCTTTATC CGGTCATAGA GGTGCTTTTT	720
	AGTATCCTTA GGCGCAAAAT AAAACGCCAG AAAGCCACCA TGCCGGATAA TTTGCATTTG	780
55	CACACCCTTT TATTTAAATT CTTGCAACAA CGCTCTTTCA ATTACCCTAA CCCTTTATGC	840
כנ	GCGTTTATCC TTATTCTATG CAACCTGCCT TTTATTTATATTATA	000

GCGTTTATCC TTATTCTATG CAACCTGCCT TTTATTTTAA TAAGCGTTTT GTTTCGCTTG

	GCTTATTTGA ATAGGCAAGT TTGCGCTTTA GAAAAGCGGG CGTTTTAA	960 1008
		1000
5	(2) INFORMATION FOR SEQ ID NO:29:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 291 base pairs	
•	(B) TYPE: nucleic acid	
10	(C) STRANDEDNESS: double	
10	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
15	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
20	(A) ORGANISM: Helicobacter pylori	
20	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1291	
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:	
30	ATGAAAAAGG TTATTGTGGC TTTAGGCGTT TTGGCGTTCG CAAATGTTTT AATGGCAACC GATGTTAAGG CTCTTGTAAA AGGTTGTGCC GCTTGCCATG GGGTTAAGTT TGAAAAGAAA GCTTTAGGTA AAAGCAAAAT CGTTAACATG ATGACCAAAA AAGAGATTGA AGAGATCTT AAAGCGGTGC CAACAAGAAT CCTGTCATGA CCGCGCAAGC TAAAAAAATTA AGCGGTGAAG ACATCAAAGC TTTAGCCAAA TACATCCCCA CTCTCAAATA A	60 120 180 240 291
	(2) INFORMATION FOR SEQ ID NO:30:	
35	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 471 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
40	(D) TOPOLOGY: circular	•
70	(ii) MOLEGIE E ENDE DO	
	(ii) MOLECULE TYPE: DNA (genomic)	
:	(iii) HYPOTHETICAL: NO	
45		
43	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
50	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 1471	
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:	

5	GGGAAAAGCG TCCTTATTGC GAGCCTTTTA GGGGCGTTTG GGCTTAAAGA GAGCAACGCT TCAAACATTG AAGTGGAATT GATCGCGCCT TTTTTAGACA CGGAAGAATA CGGCATTTTT AGAGAAGATG AGCATGAACC CTTAGTTATT AGCGTGATTA AAAAAGAAAA AACACGCTAT TTTTTAAACC AAACAAGCCT ATCTAAAAAAC ACGCTCAAAG CGTTATTAAA GGGGCTTATT AAACGCTTAT CTAACGACAG ATTCAGCCAG AATGAACTCA ACGATATTTT AATGCTCTCC	60 120 180 240 300 360 420 471
10	(2) INFORMATION FOR SEQ ID NO:31;	
15	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 357 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
20	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
25	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
30	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1357  (xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:</pre>	
35	TTAAATGATT TTGTTTTTGG TATAGAAGTG GGGCTTGATA GCAATGCGAG AAAAAATCGT AGCAGAAAGG CTATGGAAAA TCATCTTATC GGTCTTTTTG TCCAAGCTCA ATTAAATTTT AAAGAACAAG TAGATATTAG AGAATTTGAG GATTTACGCC AGGCTTTTGG AAATGATACT	60 120 180 240 300
40	(2) INFORMATION FOR SEQ ID NO:32:	
45	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 1068 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
50	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
55	(A) ORGANISM: Helicobacter pylori	

```
(ix) FEATURE:
               (A) NAME/KEY: misc_feature
                (B) LOCATION 1...1068
  5
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:
      ATGAATATCA AAATTTTAAA AATATTAGTT GGAGGGTTAT TTTTTTTGAG CTTGAACGCC
      CATTTATGGG GGAAACAAGA CAATAGCTTT TTAGGGATTG GTGAAAGAGC CTATAAAAGC
                                                                          120
      GGGAATTATT CTAAAGCGGC GTCTTATTTT AAAAAAGCAT GCAACGATGG GGTGAGTGAA
 10
                                                                          180
      GGCTGCACGC AATTAGGAAT CATTTATGAA AACGGGCAAG GCACTAGAAT AGATTATAAA
                                                                          240
     AAAGCCCTAG AATATTATAA AACCGCATGC CAGGCTGATG ATAGGGAAGG GTGTTTTGGC
                                                                          300
      TTAGGGGGGC TTTATGATGA GGGTTTAGGC ACGGCTCAAA ATTATCAAGA AGCCATTGAC
                                                                          360
     GCTTACGCTA AGGCATGCGT TTTAAAACAC CCTGAGAGTT GCTACAATTT AGGCATCATT
                                                                          420
     TATGATAGAA AAATCAAAGG CAATGCCGCT CAAGCGGTTA CTTACTATCA AAAAAGCTGT
15
                                                                          480
     AATTTTGATA TGGCTAAGGG GTGTTATATT TTAGGCACTG CCTATGAAAA AGGCTTTTTA
                                                                          540
     GAAGTCAAAC AGAGCAACCA TAAAGCCGTT ATCTATTATT TGAAAGCGTG CCGATTGAAT
     GAGGGGCAGG CTTGCCGAGC GTTAGGGAGT TTGTTTGAAA ATGGCGATGC AGGGCTTGAT
     GAAGATTTTG AAGTGGCGTT TGATTATTTG CAAAAAGCTT GCGCTTTAAA CAATTCTGGT
     GGTTGCGCGA GTTTAGGCTC TATGTATATG TTGGGCAGGT ATGTTAAAAA AGACCCCCAA
20
     AAGGCTTTTA ACTATTTCAA GCAAGCATGC GATATGGGGA GCGCGGTGAG TTGCTCTAGG
                                                                          840
     ATGGGCTTTA TGTATTCGCA AGGGGACACT GTTTCAAAAG ACTTGAGGAA AGCCCTTGAT
                                                                          900
     AATTATGAAA GAGGTTGCGA TATGGGCGAT GAAGTGGGTT GCTTCGCTCT AGCGGGCATG
                                                                         960
     TATTACAACA TGAAAGATAA AGAAAACGCC ATAATGATTT ATGACAAGGG CTGTAAATTG 1020
25
     GGCATGAAAC AGGCATGCGA AAATCTCACC AAACTCAGGG GGTATTAG
                                                                        1068
     (2) INFORMATION FOR SEQ ID NO:33:
         (i) SEQUENCE CHARACTERISTICS:
30
               (A) LENGTH: 582 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
35
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
40
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
45
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...582
       (xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:
    ATGAAAGAAA AAAACTTTTG GCCTTTAGGA ATCATGAGCG TGCTTATTTT TGGGCTTGGG
50
                                                                         60
    ATCGTGGTGT TTTTAGTGGT GTTTGCCCTA AAAAATTCGC CTAAAAATGA TTTAGTGTAT
                                                                         120
    TTCAAGGGTC ATAACGAAGT GGATTTAAAC TTTAACGCCA TGCTTAAAAC TTATGAAAAC
                                                                         180
    TTTAAATCCA ATTATCGTTT TTCAGTGGGT TTAAAGCCTC TTACCGAAAG CCCTAAAACC
                                                                         240
    CCCATTTTGC CCTATTTTTC TAAAGGCACG CATGGGGGATA AAAAAATCCA AGAAAACCTT
```

TTAAACAACG CTTTGATTTT AGAAAAGTCC AACACGCTTT ATGCACAATT GCAACCGCTC

(iii) HYPOTHETICAL: NO

5	AAACCCGCTT TAGATTCGCC AAATATTCAA GTGTATTTAG CGTTCTATCC CAGCCAATCC CAGCCCAGAT TATTAGGAAC GCTTGATTGT AAAAACGCAT GCGAACCTTT AAAATTTGAT TTGTTAGAGG GCGATAAAGT GGGGCGCTAT AAGATCCTTT TTAAATTTGT TTTTAAAAAT AAAGAAGAAT TGATTTTGGA GCAACTGGCT TTTTTTAAGT AG	420 480 540 582
	(2) INFORMATION FOR SEQ ID NO:34:	
10	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 870 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
15	(ii) MOLECULE TYPE: DNA (genomic)	• .
- 7,	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
20	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	•
	(ix) FEATURE:	
25	(A) NAME/KEY: misc_feature (B) LOCATION 1870	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:	
30	TTGGGTATCA ATATGTGTTC TAAAAAAATA AGAAATCTCA TTTTATGCTT TGGTTTTATT TTAAGCTTGT GCGCTGAAGA AAATATCACC AAAGAAAACA TGACTGAAAC GAACACGACT GAAGAAAACA CCCCTAAAGA CGCTCCCATT CTTTTGGAAG AAAAACGCGC CCAAACTCTA	60 120 180
35	GAGCTTAAAG AAGAAAATGA AGTGGCAAAA AAGATTGATG AAAAAAGCCT GCTTGAAGAA ATCCATAAGA AAAAACGCCA GCTTTACATG CTCAAAGGGG AATTGCATGA AAAGAATGAA TCCATCTTAT TCCAACAAAT GGCTAAAAAT AAGAGCGGCT TTTTTATAGG CGTGATCCTT GGCGATATAG GGATTAACGC TAATCCTTAT GAGAAGTTTG AACTTTTAAG CAATATTCAA	240 300 360 420
	GCTTCTCCCT TGCTGTATGG TTTAAGGAGC GGGTATCAAA AGTATTTCGC TAACGGGATT AGCGCCTTAC GCTTTTATGG GGAATATTTA GGGGGGGCGA TGAAAGGGTT TAAAAGCGAT TCTTTAGCTT CTTATCAAAC CGCAAGCTTG AATATTGATC TGTTGATGGA TAAGCCTATT	480 540 600
40	GACAAAGAAA AAAGGTTTGC GTTAGGGATA TTTGGAGGCG TTGGAGTGGG GTGGAATGGG ATGTATCAAA ATTTAAAAGA GATTAGAGGG TATTCACAGC CTAACGCCTT TGGGTTGGTG TTAAATTTAG GGGTGAGCAT GACGCTCAAC CTCAAACACC GCTTTGAATT AGCCCTAAAA	660 720 780
	ATGCCTCCCT TAAAAGAAAC TTCGCAAACC TTTTTATATT ATTTTAAAAG CACTAATATT TATTATATTA GTTACAACTA TTTATTGTAA	840 870
45	(2) INFORMATION FOR SEQ ID NO:35:	1
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 2007 base pairs  (B) TYPE: public and	
50	(B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	

```
(iv) ANTI-SENSE: NO
```

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

## (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...2007

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

		•					
	ATGAGAAAAC	TATTCATCCC	ACTTTTATTA	TTCAGCGCTT	TAGAAGCGAA	CGAGAAAAAC	60
15	GGCTTTTTCA	TAGAAGCCGG	CTTTGAAACT	GGGCTATTAG	AAGGCACACA	AACGCAAGAA	120
	AAAAGACACA	CCACCACAAA	AAACACTTAC	GCAACTTACA	ATTATTTACC	CACAGACACG	180
-	ATTTTAAAAA	GAGCGGCTAA	TTTATTCACC	AATGCCGAAG	CGATTTCAAA	ייייי ממממייים	240
	TCATCTTTAT	CCCCTGTTAG	AGTGTTGTAT	ATGTATAATG	GTCAATTAAC	TATAGAAAAC	300
	TTCTTGCCTT	ATAATTTAAA	TAATGTTAAG	CTTAGTTTTA	CAGACGCTCA	AGGCAACACG	360
20	ATTGATCTAG	GCGTGATAGA	GACCATCCCC	AAACACTCTA	AGATTGTTTT	ACCCGGGGAG	420
20	GCGTTTGATA	GTTTAAAAGA	GGCGTTTGAT	AAAATTGACC	CCTATACTTT	ערוירות וויירע עריירים אייריים אייריים אייריים אייריים איירים איירים איירים איירים איירים איירים איירים איירי	480
	AAATTTGAAG	CCACTAGCAC	TTCTATTTCT	GATACTAACA	CGCAGAGGGT	GTTTGAAACG	540
	CTCAATAACA	TTAAAACAAA	TCTTATAATG	AAATATAGTA	ATGAAAATCC	AAACAATTTC	600
	AACACTTGTC	CTTACAATAA	TAATGGTAAT	ACAAAAAATG	ATTGTTGGCA	AAATTTCACC	660
35	CCACAAACCG	CAGAAGAATT	CACCAATTTA	ATGTTGAACA	TGATCGCTGT	CTTAGACTCC	720
25	CAATCTTGGG	GCGATGCGAT	CTTAAACGCT	CCTTTTGAAT	TCACTAACAG	CTCAACAGAT	780
	TGCGATAGCG	ATCCTTCAAA	ATGCGTAAAT	CCCGGAGTAA	ATGGGCGTGT	ТСАТАСТАВА	840
	GTCGATCAAC	AATATATACT	CAACAAACAA	GGTATTATTA	ATAATTTTAG	מדעממממממ	900
	GAAATTGATG	CGGTTGTTTT	AAAAAATTCA	GGGGTTGTAG	GGTTAGCCAA	TGGATATGGC	960
20	AATGATGGTG	AATATGGCAC	ATTAGGGGTA	GAAGCCTATG	CTTTAGATCC	Таааааастс	1020
30	TTTGGCAACG	ACCTTAAGAC	TATCAATTTA	GAAGATTTAA	GAACCATCTT	GCATGAATTC	1080
	AGCCACACTA	AAGGCTATGG	GCATAACGGG	AATATGACCT	ATCAAAGAGT	GCCGGTAACG	1140
	AAAGATGGTC	AAGTGGAAAA	GGATAGTAAT	GGCAAGCCAA	AAGATTCTGA	TGGCCTCCCC	1200
	TATAATGTGT	GTTCGCTTTA	TGGGGGATCC	AATCAGCCCG	CTTTCCCTAG	CAACTACCCT	1260
25	AATTCCATCT	ATCACAATTG	TGCGGATGTC	CCGGCTGGCT	TTTTAGGGGT	AACAGCAGCG	1320
35	GTTTGGCAGC	AGCTCATCAA	TCAAAACGCC	TTGCCGATCA	ACTACGCTAA	CTTGGGGAGT	1380
	CAAACAAACT	ACAACCTAAA	CGCTAGTTTA	AACACGCAAG	ATTTAGCCAA	<b>ጥጥርር አ</b> ጥርርርጥር	1440
	AGCACCATCC	AAAAAACCTT	TGTAACTTCT	AGCGTTACCA	ACCACCATTT	TTCAAACGCA	1500
	TCGCAAAGTT	TTAGAAGCCC	TATTTTAGGG	GTTAACGCTA	AAATAGGCTA	TCAAAACTAC	1560
40	TTTAATGATT	TCATAGGGTT	GGCTTATTAT	GGCATCATCA	AATACAATTA	CCCTAAACCT	1620
40	GTTAATCAAA	AAGTCCAGCA	ATTGAGCTAT	GGTGGGGGGA	TAGATTTGTT	ATTGGATTTC	1680
	ATCACCACTT	ACTCCAATAA	AAATAGCCCT	ACAGGCATTC	AAACCAAAAG	CAATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	1740
	TCATCTTTTG	GTATCTTTGG	GGGGTTAAGG	GGCTTGTATA	ACAGCTATTA	<b>ፕሮፕሮፕፕሮአ</b> ል ር	1800
	AAAGTCAAAG	GAAGCGGCAA	TTTAGATGTG	GCTACCGGGT	TGAACTACCG	СТАТАВССАТ	1860
ic	TCTAAATATT	CTGTAGGGAT	TAGCATCCCT	TTAATCCAAA	GAAAAGCTAG	CCTCCTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	1920
45	AGCGGTGGCG	ATTATACGAA	CTCTTTTGTT	TTCAATGAAG	GGGCTAGCCA	CTTTAAGGTG	1980
	TTTTTCAATT	ACGGGTGGGT	GTTTTAG				2007
				*.			,

## (2) INFORMATION FOR SEQ ID NO:36:

50

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 192 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: circular

- 115 -

	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
5	(iv) ANTI-SENSE: NO	
	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	`.
10	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1192</pre>	
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:	
20	ATGAATACAG AAATTTTAAC CATCATGTTA GTTGTCTCCG TGCTTATGGG ATTGGTAGGC TTAATAGCGT TTTTATGGGG GGTTAAAAGC GGTCAGTTTG ACGATGAAAA ACGCATGCTT GAAAGCGTGT TGTATGACAG CGCGAGCGAC TTGAACGAAG CGATTTTACA AGAAAAACGC CAAAAGAATT AA	60 120 180 192
20	(2) INFORMATION FOR SEQ ID NO:37:	
25	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 1221 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
35	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
<b>40</b>	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 11221</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:	
15	ATGGTATTTT TTCATAAGAA AATTATTTTA AATTTTATCT ATTCTTTAAT GGTTGCTTTT TTATTCCATT TATCCTATGG GGTTCTTTTA AAAGCCGATG GAATGGCTAA AAAGCAAACT CTTTTAGTGG GTGAAAGGCT TGTGTGGGAT AAGCTCACGC TGTTAGGGTT TTTAGAAAAA	60 120 180
; <b>50</b>	AACCATATCC CCCAAAAACT CTACTACAAT TTGAGCTCTC AAGATAAAGA ATTGAGTGCT GAAATCCAAA GCAATGTTAC CTACTACACT TTAAGAGATG CAAATAACAC GCTCATTCAA GCCCTTATCC CTATTAGCCA GGATTTGCAA ATCCATATTT ACAAAAAAGG AGAGGATTAT TTTTTAGACT TTATCCCCAT TGTTTTCACT CGTAAAGAAA GAACCCTCCT TCTTTCCTTA CAAACTTCGC CCTATCAAGA TATTGTCAAA GCCACCAATG ACCCCCTTTT AGCCAACCAA	240 300 360 420 480
	TTGATGAACG CGTATAAAAA AAGCGTGCCT TTTAAACGCC TAGTGAAAAA CGATAAAATC GCTATCGTTT ATACAAGGGA TTATCGTGTG GGGCAAGCGT TTGGCCAGCC GACCATCAAA ATGGCGATGG TTAGCTCTCG TTTGCACCAA TACTATCTTT TTTCCCATTC AAACGGGCGT	540 600 660
55	TATTACGATT CAAAAGCGCA AGAAGTGGCA GGGTTTTTAC TAGAAACCCC GGTGAAATAC	720

5	ACCCGCATTT CTTCGCCTTT TTCGTATGGG AGGTTCCATC CTGTTTTAAA AGTTAAACGG CCTCATTACG GCGTGGATTA TGCGGCTAAA CATGGCAGTT TGATCCATTC TGCTTCAGAC GGCCGTGTGG GTTTTATAGG GGTTAAGGCG GGTTATGGGA AGGTGGTTGA AAACAAAGGCC AATCATAGGA AGGCGGTTCG CTAACGGATT AAAAAAAGGC CCGCATTTGC ATTTTGGCGT GTATAAAAAC TCCCGCCCCA TAATCCTTT AGGCTATATC CGCACCGCTA AAAGCAAGCT GCATGGCAAA CAAAGAGAGG TTTTTTTAGA AAAAATTAGA AGAACTTTTT AAAACCCATT CTTTTGAAAA AAATTCATTT	960 1020 1080 1140
10	TATCTTTTAG AGGGTTTTTA A  (2) INFORMATION FOR SEQ ID NO:38:	1200 1221
15	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 891 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
20	(ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO	
· .	(iv) ANTI-SENSE: NO	
25	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
30	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1891	
35	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:  TTGTTTTTAG TCAAAAAAAT AGGCGTGGTA ATAATGATTT TAGTCTGCTT TTTAGCTTGC TCGCAAGAGA GCTTTATCAA AATGCAAAAA AAAGCCCAAG AGCAAGAAAA TGACGGCTCT AAACGCCCCA GCTATGTGGA TTCGGATAAT GAAGTCTTTA GCGAAACGAT TTTTTTACAA AACATGGTGT ATCAGCCTAT AGAGGAAAGA AACGCTTTTT TCCAACTGAC TAAAGATGAA	60 120 180 240
40	GACAATTCTT TTAACCCTGA AAATTCCGTG ATTTTACTGA ATGAGCCAAG CGATAATAGT GAAAAAAACC TACTCTCATA CCCAAACGAT CCCAATAACA ATGAAGACAA CGCTAATAAT AGTCAAAAAA ATCCGTTCCT TTACAAGCCC AAAAGAAAAA CAAAAAACCC AAAACTCATT GAATATTCCC AACAAGATT CTACCCCCTA AAAATGGGG ATATTATCAT GAGTAAAGAA GGGGATCAAT GGTTGATAGA AACCCAAAGAAA	300 360 420
45	AACGATAAAG ATCGCCAGAT CCAAACTTC AAAGCCTTGA AGCGTTTTT AAAAGATCAA CAAATTAAGG GCAAAATTC TTCGTATGTT TATACCACCA ATAACGGTAG CTTGAGTTTA AGGCCTTTTT ATGAATCGTT TTTGTTAGAA AAAAAGAGCG ATAATGTTTA TACGATAGAG AATAAGGCTT TAGATACTAT GGAGATTTCA AAGTGTCAAA TGGTGTTAAA AAAAGCATTCA ACCGATAAAT TAGACAGCCA GCATAAAGCC ATCAGTATTC ATTTCCATTTT	480 540 600 660 720 780 840
50	CGCTTTAAGA GCGATACGGA ACTCTTTTTA GAATGTCTTA AGGAAAGTTA G  (2) INFORMATION FOR SEQ ID NO:39:	891
55	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 747 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li></ul>	·

	(D) TOPOLOGY: circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
5	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
10	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
15	(B) LOCATION 1747	
13	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:	
	GTGAGCTATG ACAACACCGA TGATTATTAT TTCCCTAGAA ATGGGGTTAT CTTTAGTTCC	60
	TATGCGACAA TGTCTGGTTT GCCAAGCTCT GGCACGCTCA ATTCTTGGAA CGGGTTAGGC	120
20	GGGAATGTCC GTAACACCAA AGTTTATGGT AAATTCGCCG CTTACCACCA TTTGCAAAAA	180
	TATTTATTGA TAGATTTGAT CGCTCGTTTT AAAACGCAAG GGGGCTATAT CTTTAGGTAT	240
	AACACCGATG ATTACTTGCC CTTAAACTCC ACTTTCTACA TGGGGGGCGT AACCACGGTG AGAGGCTTTA GGAACGGCTC AATCACACCT AAAGATGAGT TTGGCTTGTG GCTTGGAGGC	300
	GATGGGATTT TTACCGCTTC TACTGAATTG AGCTATGGGG TGTTAAAAGC GGCTAAAATG	360 420
25	CGTTTAGCGT GGTTTTTTGA CTTTGGTTTC TTAACCTTTA AAACCCCAAC TAGGGGGAGT	480
	TTCTTCTATA ACGCTCCCAC CACGACGGCG AATTTTAAAG ATTATGGCGT TGTAGGGGCT	540
	GGGTTTGAAA GGGCGACTTG GAGGGCTTCT ACAGGCTTAC AGATTGAATG GATTTCGCCC	600
	ATGGGGCCTT TGGTGTTGAT TTTCCCTATA GCGTTTTTCA ACCAATGGGG CGATGGCAAT	660
	GGCAAAAAAT GTAAAGGGCT GTGCTTTAAC CCTAACATGA ACGATTACAC GCAACATTTT	720
30	GAATTTTCTA TGGGAACAAG GTTTTAA	747
	(2) INFORMATION FOR SEQ ID NO:40:	
	(i) SEQUENCE CHARACTERISTICS:	
35	(A) LENGTH: 1008 base pairs	
	(B) TYPE: nucleic acid	
•	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
10	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
15	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
50	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11008	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:	
55	GTGCAACACT TCAATTTCCT CTATAAAGAT TCTTTATTTT CTATCGCTTT ATTCACTTTC	60

	ATTATCGCTC TTGTGATTTT ATTAGAACAG GCTAGAGCGT ATTTCACCCG AAAGAGAAAC	120
	AAAAAATTTT TGCAAAAATT CGCCCAAAAT CAAAACGCCT ATGCGAGCAG CGAGAATTTA	180
	GACGAGCTTT TAAAGCATGC TAAAATTTCC AGTTTGATGT TTTTAGCTAG GGCGTATTCT	240
	AAAGCGGATG TGGAAATGAG CATTGAAATC TTAAAAGGGC TTTTGAATCG CCCCTTAAAA	300
5	GATGAAGAAA AAATCGCTGT TTTAGATTTA TTGGCTAAAA ATTATTTTAG CGTGGGGTAT	360
	TTGCAGAAAA CAAAAGACAC CGTGAAAGAA ATTTTGCGCT TTTCCCCAAG GAATGTGGAA	420
	GCGTTGTTGA AGCTTTTGCA TGCGTATGAA TTAGAAAAAG ATTATTCAAA GGCTTTAGAA	480
	ACTITGGAAT GTTTGGAAGA ATTAGAGGTG CCTAAAATTG AAACGATTAA AAATTACCTC	
	TATTTAATGC ATTTAATAGA GAATAAGGAA GATGCGGCTA AAATCTTGCA TGTTTCAAAA	540
. 10	GCGTCGTTAG ATTTGAAAAA AATCGCTCTG AATCACTTAA AATCGCATGA TGAAAATCTT	600
	TTTTGGCAAG AAATTGATAC AACCGAACGG CTAGAAAATG TGATCGATCT TTTATGGGAT	660
	ATGAATATCC CTGCTTTTAT TTTAGAAAAA CATGCCCTTT TGCAGGACAT CGCGCGATCT	720
	CAAGGGTTGC TTTTGGATCA CAAACCTTGC CAAATTTTTG AATTAGAGGT TTTACGCGCT	780
	CTATTGCATA GCCCTATAAA AGCGAGTCTG ACTTTTGAAT ACCGCTGCAA GCATTGCAAA	
15	CAAATCTTTC CTTTTGAAAC CCATACCTCT CCTCTTTGAAT ACCGCTGCAA GCATTGCAAA	900
	CAAATCTTTC CTTTTGAAAG CCATAGGTGT CCTGTGTGTT ACCAGTTAGC GTTTATGGAT ATGGTGCTTA AAATCTCTAA AAAAACGCAT GCTATGGGAG TGGATTAA	960
	AIGGIGCITA MAMICICIAM AMMANCGCAT GCTATGGGAG TGGATTAA	1008
	(2) INFORMATION FOR SEQ ID NO:41:	
20		
20	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1242 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
25	(D) TOPOLOGY: circular	
23	(24) MATTERWAY TO THE AND THE	
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(III) HIPOTHETICAL: NO	
30	(iv) ANTI-SENSE: NO	
-	(IV) ANII-BENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(A) ORGANISM: Helicopacter pylori	
35	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11242	
	(b) DOCATION 11242	
	(vi) CENTENGE DECORTEMENT CO	
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:	
	ATCACCAAAA TITTITUUTGUTTA TIATITUTGUTTA A	
	ATGAGGAAAA TTTTTTCTTA TATTTCTAAG GTTCTATTAT TTATTGGGGT GGTTTATGCA	60
	GAGCCTGATT CTAAAGTGGA AGCCTTAGAA GGGAGGAAGC AAGAGTCTTC TTTGGATAAA	120
,	AAAATCCGCC AAGAATTGAA GAGTAAGGAA TTGAAGAATA AGGAATTAAA GAATAAGGAT	180
45	TTGAAAAATA AAGAAGAAAA GAAAGAAACA AAAGCCAAGA GAAAACCCAG AGCAGAAGTC	240
7.7	CATCATGGGG ACGCCAAAAA TCCCACTCCA AAGATCACGC CTCCTAAAAT CAAAGGGAGT	300
	AGTAAGGGCG TTCAAAATCA AGGCGTTCAA AACAACGCGC CAAAACCTGA AGAAAAAGAT	360
	ACAACCCCTC AAGCTACTGA AAAAAATAAG GAAACAAGCC CTAGCTCTCA ATTCAATTCC	420
	ATTTTGGTA ATCCTAATAA CGCTACCAAC AACACCCTTG AAGATAAGGT CGTAGGGGGC	480
50	ATTTCATTGC TTGTTAATGG TTCGCCTATC ACGCTGTATC AAATCCAAGA AGAGCAAGAA	540
50	AAATCTAAAG TGAGTAAGGC TCAAGCTAGG GATCGTTTGA TCGCTGAACG CATTAAAAAC	600
	CAAGAAATTG AGCGCTTAAA AATCCATGTA GATGATGACA AGCTAGACCA AGAAATGGCG	660
•	ATGATGGCGC AACAACAAGG CATGGATTTA GACCATTTCA AACAGATGCT TATGGCTGAG	720
	GGGCATTATA AACTCTATAG AGATCAACTT AAAGAGCATT TAGAAATGCA AGAATTGTTG	780
<i></i>	CGTAATATTT TGCTCACGAA TGTGGATACC AGCTCTGAAA CCAAAATGCG CGAATATTAC	840
55	CGTAATATTT TGCTCACGAA TGTGGATACC AGCTCTGAAA CCAAAATGCG CGAATATTAC AACAAACACA AGGAGCAATT CAGTATCCCC ACAGAAATAG AAACCGTGCG CTACACTTCC	

- 119 -

_	ATTTCGCATG AGCAAGGCTC TTTCACGCCC GTTATGAATG GGGGTGGGGG GCAGTTCATC	960 1020 1080 1140
5	TTCATCGCCC AAAAATTAGT GGAAGAATCT AAGGATAAGA TTTTAGAAGA GCATTTTGAA	1200 1242
	(2) INFORMATION FOR SEQ ID NO:42:	
10	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 561 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
15	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
20	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
25	(ix) FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 1561	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:	•
	ATGATTAAAA GAATTGCTTG TATTTTAAGC TTGAGCGCGA GTTTAGCGTT AGCTGGCGAA GTGAATGGGT TTTTCATGGG TGCGGGTTAT CAACAAGGTC GTTATGGCCC TTATAACAGC AATTACTCTG ATTGGCGTCA TGGCAATGAC CTTTATGGTT TGAATTTCAA ATTAGGTTTT GTAGGCTTTG CCAATAAATG GTTTGGGGCT AGGGTGTATG GCTTTTTAGA TTGGTTTAAC	60 120 180
35	ACTTCAGGGA CTGAACACAC CAAAACCAAT TTGCTCACCT ATGGCGGCGG TGGCGATTTG ATTGTCAATC TCATTCCTTT GGATAAATTC GCTCTAGGTC TCATTGGTGG CGTTCAATTA GCCGGAAACA CTTGGATGTT CCCTTATGAT GTCAATCAAA CCAGATTCCA GTTCTTATGG	240 300 360 420
40	AATTTAGGCG GAAGAATGCG TGTTGGGGAT CGCAGTGCGT TTGAAGCGGG CGTGAAATTC CCTATGGTTA ATCAGGGTAG CAAAGATGTA GGGCTTATCC GCTACTATTC TTGGTATGTG GATTATGTCT TCACTTTCTA G	480 540 561
	(2) INFORMATION FOR SEQ ID NO:43:	
45	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 729 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li></ul>	
50	(D) TOPOLOGY: circular  (ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
55	(iv) ANTI-SENSE: NO	

480

```
(vi) ORIGINAL SOURCE:
           (A) ORGANISM: Helicobacter pylori
          (ix) FEATURE:
 5
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...729
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:
     ATGAAAAAT TTTTTCTCA ATCTTTGTTA GCTCTTATTA TCTCTATGAA TGCGGTATCT
     GGCATGGATG GTAATGGCGT TTTTTTAGGG GCGGGTTATT TGCAAGGACA GGCGCAAATG
                                                                          120
     CATGCGGATA TTAATTCTCA AAAACAAGCC ACCAACGCTA CGATCAAAGG CTTTGACGCG
                                                                          180
     CTCTTGGGGT ATCAATTTT CTTTGAAAAA CACTTTGGCT TACGCCTTTA TGGGTTTTTT
                                                                          240
     GACTACGCTC ATGCCAATTC TATTAAGCTT AAAAACCCTA ACTATAATAG CGAAGCGGCG
                                                                          300
     CAAGTGGCTA GTCAAATTCT TGGGAAACAA GAAATCAATC GTTTAACAAA CATTGCCGAT
                                                                          360
     CCCAGAACTT TTGAGCCGAA CATGCTCACT TATGGGGGGG CTATGGACGT GATGGTTAAT
                                                                          420
     GTCATCAATA ACGGCATCAT GAGTTTGGGG GCTTTTGGCG GGATACAATT GGCCGGCAAT
                                                                          480
     TCATGGCTTA TGGCGACACC GAGCTTTGAG GGCATTTTAG TGGAACAAGC CCTTGTGAGC
                                                                          540
     AAGAAAGCCA CTTCTTTCCA ATTTTTATTC AATGTGGGGG CTCGCTTAAG GATCTTAAAA
                                                                          600
20
     CATTCTAGCA TTGAAGCGGG CGTGAAATTC CCCATGCTAA AGAAAAACCC CTACATCACT
                                                                          660
     GCAAAAAATT TGGATATAGG GTTTAGGCGC GTGTATTCGT GGTATGTGAA TTACGTGTTC
                                                                          720
     ACTTTCTAG
                                                                          729
     (2) INFORMATION FOR SEQ ID NO:44:
25
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 771 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
30 -
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
35
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
40
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...771
45
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:
     ATGGGATACG CAAGCAAATT AGCTTTAAAG ATTTGTTTGG TAGGTTTATG TTTATTTAGC
     ACCCTTGGTG CAGAACACCT TGAGCAAAAA GGGAATTATA TTTATAAGGG AGAGGAGGCT
                                                                         120
     TATAATAATA AGGAATATGA GCGAGCGCT TCTTTTTATA AGAGCGCTAT TAAAAATGGT
                                                                         180
50
    GAGTCGCTTG CTTATATTCT TTTAGGGATC ATGTATGAAA ATGGTAGGGG TGTACCTAAA
                                                                         240
    GATTACAAGA AAGCGGTTGA ATATTTCCAA AAAGCTGTTG ATAACGATAT ACCTAGAGGG
                                                                         300
     TATAACAATT TGGGCGTGAT GTATAAAGAG GGTAAGGGAG TTCCTAAAGA TGAAAAGAAA
                                                                         360
     GCGGTGGAAT ATTTTAGAAT AGCTACAGAG AAAGGTTATA CTAACGCTTA TATCAACTTA
                                                                         420
    GGCATCATGT ATATGGAGGG CAGGGGAGTT CCAAGTAACT ATGCGAAAGC GACAGAATGT
```

TTTAGAAAAG CGATGCATAA GGGCAATGTG GAAGCTTATA TTCTCCTAGG GGATATTTAT

55

1380

1440

1500

1560

	TATAGCGGGA ATGATCAATT GGGTATTGAG CCGGACAAAG ATAAGGCTGT TGTCTATTAT AAAATGGCGG CTGATGTAGA TTCTTCTAGA GCTTATGAAG GGTTGTCAGA GTCTTATCGG TATGGGTTAG GCGTGAAAA AGATAAAAAA AAGGCTGAAG AATACATGCA AAAAGCATGC GATTTTGACA TTGATAAAAA TTGTAAGAAA AAGAACACTT CAAGCCGATA A	600 660 720 771
5	(2) INFORMATION FOR SEQ ID NO:45:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1974 base pairs	
10	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
15	(ii) MOLECULE TYPE: DNA (genomic)	
15	(iii) HYPOTHETICAL: NO	
	(III) HIPOIREITCAE: NO	
	(iv) ANTI-SENSE: NO	
20	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	•
	(A) NAME/KEY: misc feature	
25	(B) LOCATION 11974	
•	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:	
	ATGAGAAAAC TATTCATCCC ACTTTTATTA TTCAGCGCTT TAGAAGCGAA CGAGAAAAAC	60
30	GGCTTTTTCA TAGAAGCCGG CTTTGAAACT GGGCTATTAG AAGGCACACA AACGCAAGAA	120
	AAAAGACACA CCACCACAAA AAACACTTAC GCAACTTACA ATTATTTACC CACAGACACG	180
	ATTTTAAAAA GAGCGGCTAA TTTATTCACC AATGCCGAAG CGATTTCAAA ATTAAAATTC	240
	TCATCTTTAT CCCCTGTTAG AGTGTTGTAT ATGTATAATG GTCAATTAAC TATAGAAAAC	300
35	TTCTTGCCTT ATAATTTAAA TAATGTTAAG CTTAGTTTTA CAGACGCTCA AGGCAATGTG ATCGATCTAG GCGTGATAGA GACTATCCCC AAACACTCTA AGATTGTTTT GCCCGGAGAG	360
55	GCATTTGATA GTCTAAAAAT TGACCCCTAT ACTTTATTTC TTCCAAAAAT TGAAGCCACT	420 480
	AGCACTTCTA TTTCTGACGC TAACACGCAG AGGGTGTTTG AAACGCTCAA TAAGATTAAG	540
	ACAAATTTGG TCGTAAATTA TAGGAATGAA AACAAATTTA AAGATCACGA AAATCATTGG	600
	GAAGCCTTTA CCCCACAAAC CGCAGAAGAA TTCACTAATT TAATGTTGAA CATGATCGCT	660
40	GTTTTAGACT CCCAATCTTG GGGCGATGCG ATCTTAAACG CTCCTTTTGA GTTCACTAAC	720
	AGCCCAACAG ATTGCGATAA TGATCCTTCA AAATGCGTAA ATCCTGGGAC AAACGGGCTT	780
	GTCAATTCTA AAGTCGATCA AAAATATGTG TTAAACAAAC AAGACATTGT CAATAAATTT	840
•	AAAACAAAG CGGATCTTGA TGTAATTGTT TTAAAGGATT CAGGGGTTGT AGGGCTTGGG	900
45	AGTGATATTA CCCCTAGCAA CAATGATGAT GGCAAGCATT ATGGCCAGTT AGGGGTAGTA	960
<del>1</del> J	GCTTCTGCTT TAGATCCTAA AAAACTCTTT GGCGATAACC TTAAGACTAT CAATTTAGAG GATTTAAGAA CCATCTTGCA TGAATTCAGC CACACTAAAG GCTATGGGCA TAACGGGAAT	1020
	ATGACCTATC AAAGAGTGCC GGTAACGAAA GATGGTCAAG TGGAAAAGGA TAGTAATGGC	1080 1140
	· · · · · · · · · · · · · · · · ·	1200
		1260
50	GCTGGCTTTT TAGGGGTAAC AGCAGCGGTT TGGCAGCAGC TCATCAATCA AAACGCCTTG	

CCGATCAACT ACGCTAACTT GGGGAGTCAA ACAAACTACA ACCTAAACGC TAGTTTAAAC

ACGCAAGATT TAGCCAATTC CATGCTCAGC ACCATCCAAA AAACCTTTGT AACTTCTAGC

GTTACCAACC ACCATTTTC AAACGCATCG CAAAGTTTTA GAAGCCCTAT TTTAGGGGTT

AACGCTAAAA TAGGCTATCA AAACTACTTT AATGATTTCA TAGGGTTGGC TTATTATGGC

ATCATCAAAT ACAATTACGC TAAAGCTGTT AATCAAAAAG TCCAGCAATT GAGCTATGGT

5	GGGGGGATAG ATTTGTTATT GGATTTCATC ACCACTTACT CCAATAAAAA TAGCCCTACA GGCATTCAAA CCAAAAGGAA TTTTTCTTCA TCTTTTGGTA TCTTTTGGGG GTTAAGGGGC TTGTATAACA GCTATTATGT GTTGAACAAA GTCAAAGGAA GCGGCAATTT AGATGTGGCT ACCGGGTTGA ACTACCGCTA TAAGCATTCT AAATATTCTG TAGGGATTAG CATCCCTTTA ATCCAAAGAA AAGCTAGCGT CGTTTCTAGC GGTGGCGATT ATACGAACTC TTTTGTTTTC AATGAAGGGG CTAGCCACTT TAAGGTGTTT TTCAATTACG GGTGGGTGTT TTAG	1680 1740 1800 1860 1920 1974
	(2) INFORMATION FOR SEQ ID NO:46:	
10	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 504 base pairs (B) TYPE: nucleic acid	
* .	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
15		
	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
20.	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
25	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1504</pre>	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:	
	ATGAAATTGG TGAGTCTTAT TGTAGCGTTA GTTTTTTGTT GTTTTTTAGG GGCTGTAGAG TTGCCTGGAG TTTATCAAAC TCAAGAATTT TTATACATGA AAAGCTCTTT TGTGGAGTTT TTTGAGCATA ACGGGAAGTT CTATGCCTATA GGTATTTCTG ATGTGGATGG CTCTAAAGCC	60 120 180
35	AAAAAAGACA AACTCAATCC TAACCCAAAG CTAAGGAATC GCAGCGATAA AGGCGTGGTG TTTTTAAGCG ATTTGATTAA GGTTGGGGAA CAATCTTATA AAGGCGGTAA GGCGTATAAT	240 300
	TTCACTTCAA GCTATGACAA ATGGGGGTAT GTGGGCAAAA CCTTCACCTC CAAACGGTTT	360 420
	AGCGATGAAG AAATCAAAAA TCTAAAGCTC AAGCGTTTTA ACTTGGACGA AGTCCTTAAA ACCCTCAAAG ATAGCCCTAT TTAA	480
40	(2) INFORMATION FOR SEQ ID NO:47:	504
•	(i) SEQUENCE CHARACTERISTICS:	
45	(A) LENGTH: 885 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
50	(ii) MOLECULE TYPE: DNA (genomic)	
, <b>50</b>	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
55	(vi) ORIGINAL SOURCE:	

```
(A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
 5
               (B) LOCATION 1...885
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:
     ATGAGTAATC AAGCGAGCCA TTTGGATAAT TTTATGAACG CTAAAAATCC CAAAAGTTTT
                                                                           60
     TTTGATAATA AGGGGAATAC CAAATTCATC GCTATCACAA GCGGTAAGGG GGGCGTGGGG
                                                                          120
     AAATCCAACA TTAGCGCTAA TTTAGCTTAC TCTTTATACA AGAAAGGTTA TAAGGTAGGG
     GTATTTGATG CGGATATTGG TTTAGCGAAT TTAGATGTCA TTTTTGGGGT GAAAACCCAT
     AAAAATATCT TGCATGCCTT AAAAGGCGAA GCCAAATTGC AAGAAATCAT TTGCGAGATT
     GAACCCGGGC TTTGCTTAAT CCCTGGGGAT AGCGGCGAAG AAATTTTAAA ATACATCAGC
15
     GGCGCGGAAG CTTTGGATCG ATTCGTAGAT GAAGAGGGGG TTTTAAGCTC TTTAGATTAT
                                                                          420
     ATTGTGATTG ATACGGGTGC TGGGATTGGG GCCACTACGC AAGCGTTTTT GAATGCGAGC
                                                                          480
     GATTGCGTGG TGATTGTTAC CACACCCGAT CCTTCAGCGA TTACCGATGC GTATGCATGC
     ATTAAAATCA ACTCCAAGAA TAAAGATGAA TTGTTCCTTA TCGCTAACAT GGTAGCCCAA
                                                                          600
     CCTAAAGAAG GCAGGGCGAC TTATGAAAGG CTATTCAAGG TGGCTAAAAA CAATATCGCT
                                                                          660
     TCATTAGAAT TGCACTATTT AGGGGCGATT GAAAACAGCT CCTTATTGAA ACGCTATGTG
                                                                          720
     AGGGAGCGAA AGATTTTGAG GAAAATAGCC CCTAACGATT TGTTTTCGCA ATCCATTGAC
                                                                          780
     CAGATAGCGA GCCTTTTAGT TTCTAAACTA GAAACCGGCA CTTTAGAAAT ACCAAAAGAA
                                                                          840
     GGTTTAAAAA GCTTTTTTAA AAGGCTTTTG AAGTATTTGG GGTAG
                                                                          885
25
     (2) INFORMATION FOR SEQ ID NO:48:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 1119 base pairs
               (B) TYPE: nucleic acid
30
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
35
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
40
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...1119
45
        (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:
    TTGGAACCTT CAAGAAATCG CCTAAAACAT GCCGCCTTTT TTGTGGGGCT TTTTATCGTT
    TTGTTTTAA TTATAATGAA GCACCAAACC TCCCCCTATG CTTTCACGCA TAATCAAGCC
50°
    CTTGTCACTC AAACCCCCCC CTATTTCACG CAACTCACTA TCCCTAAACC AAATGACGCT
                                                                          180
    TTAAGCGCGC ATGCGAGCTC TTTAATCAGC TTGCCTAACG ACAATCTTTT GAGCGCTTAT
                                                                          240
    TTTAGCGGCA CTAAAGAAGG GGCAAGGGAT GTGAAAATCA GCGCGAATCT TTTTGACAGC
                                                                          300
```

AAGACTAATC GCTGGAGCGA AGCCTTCATT CTTTTAACCA AAGAAGAGCT TTCTCATCAT

TCGCATGAAT ACATCAAAAA ATTAGGTAAC CCCTTGCTTT TTTTGCATGA TAATAAAATT TTGTTGTTTG TCGTAGGGGT GAGCATGGGC GGGTGGGCCA CTTCTAAAAT CTATCAATTT

	· · · · · · · · · · · · · · · · · · ·	
	GAAAGCGCTT TAGAGCCGAT TCATTTTAAG TTTGCGCGAA AACTCTCTTT AAGCCCTTTT	F 4 6
	TTAAATTTGA GCCATTTAGT AAGGAATAAG CCTTTTAAACA CCACTGATGG CGGGTTTATG	540
	CTACCACTCT ATCACGAATT AGCCACCCAA TACCCCTTGT TGTTGAAATT TGACCAACAA	600
	AATAACCCAA GAGAGCTTTT AAGGCCTAAT ACCTTAAACC ACCAGCTCCA ACCAAGCTTA	660
5	ACCCCTTTA AMBICTORIC TOTTOMOGOGO TOTTOMOGO TOTTOMOGOGO	720
	ACCCCCTTTA AAGACTGCGC TGTCATGGCG TTTAGAAACC ATTCTTTAA AGATAGCCTC	780
100	ATGCTAGAAA CCTGTAAAAC CCCCACTGAT TGGCAAAAAC CCATTTCTAC AAATCTTAAA	840
- '	AACTTAGATG ATTCTTTAAA TTTACTCAAT TTAAATGGAA TATTGTATTT GATCCACAAC	900
	CCTAGCGATT TATCACTGCG TCGTAAAGAA CTTTGGCTTT CTAAATTAGA AAACTCCAAC	960
10	TCGTTTAAAA CCTTAAAAGT TTTGGATAAA GCGAATGAAG TGAGTTACCC AAGCTATAGC	1020
10	CTTAATCCGC ATTTTATAGA TATTGTCTAT ACTTACAACC GCTCTCATAT CAAACACATC	1080
	CGTTTCAATA TGGCTTATTT AAATTCCCTT CTCAAGTGA	1119
-	(2) INFORMATION FOR SEQ ID NO:49:	
15	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 2937 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
20		,
	(ii) MOLECULE TYPE: DNA (genomic)	
	(genomic)	
	(iii) HYPOTHETICAL: NO	
25	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(4) ONGILION: MCIICODACCEI PYIOTI	
30	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 12937	
	(-,,,,,,,,,, _	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:	
35	5-5011110W. 5EQ ID NO:49:	
	ATGAAGAAAA GAAAACATGT ATCCAAGAAA GTGTTTAATG TCATTATCTT GTTTGTGGCA	
•	GTATTCACTC TTTTAGTCGT CATTCACAAA ACCCTTTCAA ACGGCATTCA CATACAAAAT	60
	TTAAAAATTG GAAAACTTGG CATTTGTGAA GCCCTTTCAA ACGGCATTCA CATACAAAAT	120
	TTAAAAATTG GAAAACTTGG CATTTCTGAA TTATACTTAA AACTCAATAA CAAGCTTTCT	180
40	TTGGAAGTTG AGCGGGTTGA TCTCTCTTCT TTCTTCCATC AAAAACCCAC TAAAAAGCGT	240
	TTAGAAGTTT CTGATTTGAT TAAAAATATC CGTTATGGCA TTTGGGCGGT GTCTTATTTT	- 300
	GAAAAACTTA AAGTCAAAGA AATCATTTTA GACGATAAAA ATAAAGCCAA TATCTTTTTT	360
	GATGGGAATA AATACGAGTT AGAATTTCCA GGAATCAAAG GGGAATTTTC CCTAGAAGAC	420
	GATAAAAATA TCAAGCTTAA AATCATCAAT TTGCTTTTTA AAGATGTTAA AGTCCAAGTG	480
45	GATGCCAACG CCCACTATTC ACCCAAAGCC AGGAAAATGG CGTTCAATTT GATTGTCAAG	540
73	CCCTTAGTTG AACCCAGCGC TGCAATTTAT TTGCAAGGGC TAACCGATTT AAAAACCATA	600
	GAATTAAAAA TTAACACTTC TCCAATGAAA AGCCTAGCGT TTTTAAAGCC TCTTTTCCAA	660
	CGCCAATCGC AAAAAAATTT AAAAACGTGG ATTTTTGACA AGATCCAATT TGCCAGCTTT	720
	AAGATTGATA ACGCTTTAAT CAAGGCTAAT TTCACTCCTA GCGAGTTTAT CCCATCCCTT	780
50	TIGGAAAATI CIGTAGTTAA AGCCACTTIG ATTAAGCCTI CAGTCGTTTT TAATGATGCC	840
50	TTATCGCCCA TTAAAATGGA TAAAACCGAA TTGATTTTCA AAAACAAACA GCTCCTCATA	900
	CAGCCCCAAA AAATCACTTA TGAAACCATG GAATTAACCG GCTCTTACGC CACTTTTTCC	960
	AATTIGITAG AAGCCCCTAA GTTGGAGGTT TTTTTAAAAA CGACCCCTAA TTATTATGCC	1020
	GATAGCATTA AGGATTTATT GAGCGCTTAT AAAGTCGTTT TACCTTTGGA TAAAATCAGC	1080
	ATGUCATUTA GUGGGGATTT GAAGCTCACT TTGCAATTCT TAAAAAACAC CGCCCCTTA	1140
55	TTTAGCGTTC AAGGCAGCGT TAATTTGCAA GAAGGCACTT TCTCGCTCTA TAATATCCCC	1200
		1200

60

120

	•						
	CTTTACACGC	AAAGCGCTCA	AATCAATTTG	GACATCGCCC	AAGAATACCA	ATACATCTAC	1260
						AATCGCTTTA	1320
						AGTCAATACC	1380
					CTCAAGAAGA		1440
5						AAATTCAGAA	
-						ATTCACTAAA	1560
					CGTTGAGTTT		1620
					TAGAAGGCGA		1680
					AGCCCTATTC		1740
10					CGAGCGATTT		1800
					ATAGGAGCGA		1860
						CTATACTCCA	1920
						TAATAACATT	1980
					CTATTGCGGG		2040
15						TTTCATTAGC	2100
	GCCAAACAAC	GCTATGAAAA	AGCCCACAAA	ATTATCCCCA	TCTCTACACG	CATCCATGCT	2160
	AAAGATGTCG	TGCTGATCTA	TAAAAAAATG	CCTTTTCCTT	TAGAAAATCT	TGATATTGTC	2220
	GCTCAAGACG	ATAGGGTGAA	AATTGATGGC	AATTATAAAA	ACGCCATGAT	CATGGCGGAT	2280
	TTAGTGCATG	${\tt GGGCTTTGTA}$	TCTTAAGGCT	CATAATTTTA	GCGGGGATTA	TATCAACACC	2340
20	ATTCTTCAAA	AAGATTTCGT	AGAAGGAGGC	TTATTCACGC	TTATTGGGGC	TCTTGAAGAT	2400.
					TAAAGAATTT		2460
					TTGTCTTTAG		2520
						CACTAAAGAA	2580
						TGGCAATGGA	2640
25					AAGTTTCCAC		2700
					${\tt TCGTTTTAGG}$		2760
						CCAAGTAACT	2820
						CACGCCTATT	2880
20	GACATCATCG	TGGATGAAGT	CAAGAAAAAC	ATTGATTCAA	AAAGGAAATT	AAAATGA	2937
30	(2) INFORMA	ATION FOR SE	Q ID NO:50:	:			
	/÷\ ct	QUENCE CHAR	)	• .			
		(A) LENGTH:				•	
35		(B) TYPE: nu	-	Jails			
, , ,		(C) STRANDEL					
		(D) TOPOLOGY					
	`	, 10101001	· Olloulul			•	
	(ii) MC	LECULE TYPE	: DNA (geno	omic)			
40	(22)			, <u></u>			
	(iii) HY	POTHETICAL:	NO	•			
	,,						
	(iv) AN	TI-SENSE: N	10	·			
	••		,			,	
45	(vi) OR	RIGINAL SOUR	CE:				
_		A) ORGANISM		ter pylori		•	
	·	,,		P,			
	(ix) FE	ATURE:					
-		A) NAME/KEY	: misc feat	ure			*
50		B) LOCATION					
						•	
•	(xi) SE	QUENCE DESC	RIPTION: SE	Q ID NO:50:			

ATGAATACTA TTATAAGATA TGCGAGTTTA TGGGGCTTGT GTATTACTCT AACTCTAGCG

CAAACCCCCT CTAAAACCCC TGATGAAATC AAGCAAATCC TTAACAATTA TAGCCATAAG

	AATTTAAAGC TCATTGATCC GCCGACAAGT TCTTTAGAAG CGACACCGGG TTTTTTACCC	180
	TCGCCTAAAG AAACAGCGAC CACGATCAAT CAAGAGATCG CTAAATACCA TGAAAAAAGC	240
	GATAAAGCCG CTTTGGGGCT TTATGAATTG CTAAAGGGGG CTACCACCAA TCTCAGTTTG	300
_	CAAGCGCAAG AACTCAGTGT CAAGCAAGCG ATGAAGAACC ACACCATCGC CAAAGCGATG	360
5	TTTTTGCCTA CTTTGAACGC GAGTTATAAT TTTAAAAATG AAGCTAGGGA TACTCCAGAA	420
•	TATAAGCATT ATAACACCCA ACAACTCCAA GCTCAAGTCA CATTGAATGT GTTTAATGGC	480
•	TTTAGCAATG TGAATAATGT CAAAGAAAAG TCTGCGACTT ACCGATCCAC TGTGGCTAAT	540
	TTAGAATATA GCCGCCAAAG CGTGTATTTG CAAGTGGTGC AACAATACTA CGAGTATTTT	600
	AACAATCTCG CTCGCATGAT CGCTTTGCAA AAGAAATTAG AGCAAATCCA AACGGACATT	660
10	AAAAGGGTTA CTAAGCTCTA TGACAAAGGG CTGACCACGA TTGATGATTT ACAAAGCTTA	720
	AAAGCGCAAG GGAATTTGAG CGAATACGAT ATTTTGGACA TGCAATTTGC TTTGGAGCAA	780
	AACCGCTTGA CTTTAGAATA CCTCACTAAC CTCAGTGTGA AAAATTTGAA AAAGACCACG	840
	ATTGATGCGC CTAATTTGCA ATTAAGAGAA AGGCAGGATT TGGTTTCTTT AAGGGAGCAG	900
	ATTTCTGCAC TCAGATACCA AAACAAGCAA CTCAATTATT ACCCCAAGAT AGATGTGTTT	960
15	CACTCATCCC TTTTTTTTCCAT CCAAAAACCC CCTTATCCC	1020
	TACCCAGGTC AGCAAAATAC GGCTGGGGTT ACTGCGACTT TGAATATTTT TGATGATATA 1	080
	CCCTTCACCT TCCAAAAACA ATCCATCATCATCA CTACCACAA T TO T	140
	GCGTATAAAA AATTGGAGCA AGAAAAAGAC GAACAGCTTT ACAGAAAGTC GCTTGATATT 1	200
	CCCACACCTA ACATTOCATOCATA ACACTA ACTOCATA ACTOCA	260
20	AATATTAAAA CCAAATACCA CCCGAAGGGGAAGGGAAG	.320
,	ACCACGCGCT TTGATGCAGA AGTGGCTTAC AATTTAGCGC TCAACAATTA CGAAGTGCAA	380
	AAACCCAATT ACATTTTTTAA CACCCCCAT AAAAAAAA	434
25	(2) INFORMATION FOR SEQ ID NO:51:  (i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 1239 base pairs  (B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
30	(D) TOPOLOGY: circular	
	(b) Totobodi. Cilcular	
	(ii) MOLECULE TYPE: DNA (genomic)	
35	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
40	pitoli	
	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
	(B) LOCATION 11239	
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:	
	ATGCTATCTT TTATAAGCGC GTTTGATAAA AGGGGCGTTT CAATACGCCT TCTAACAGCC	60
		120
	<u> </u>	
50	TOTOLAGAAA AAGTOOTTAG GAAATIGGGAT AAGGOTATI	180
	CCTAACCTCA CCCATTTTTTT CACCCTCCAT ACCACCTTTA ACCACCTTTA	240
	TTCTCTCTANN NACTOCARTOR AND COMPANY AND COMPANY	300 360
	CAAAAACAAA AAAAAAAAAAAA AAAAAAAAAAAAAA	
	ATCATAAACC CCATTCAAAA CTATAAAAAA CAAACAAA	120 180
55	ATTAAAATT TACAAAACAC CCTCTATATCAA GCCAAGCAA	540

- 127 -

	•							
	GCGATCGCCA AGTTAGAAAT TTTAAAATCG CTATTAGAAA TCCAAAAAAA CGATTTAGAA	600						
-	GTAGCGCTCT CTAGCAGCCA TTATTCCATG GGCGAATTGA CTTTTAAAGA AAACGAGATT	660						
	TTAAGCATTG CCCCTAAAAA TTTTGAATTC AATAACGAGC AAGAGCTGCA TAACATTAGC	720						
. 5	GCCACTAATT ACGATATTGC GATCGCCAGG CTTGATGAAG AAAAAGCACA AAAAGACATC	780						
3	ACTCTGGCTA AAAAAAGCTT TTTAGAAGAC ATAAACGTTA CCGGGGTGTA TTATTTCCGC TCCAAACAAT ACTATAACTA CGACATGTTT AGCGTCGCTT TGTCTATCCC TTTACCTCTT	840						
	TATGGCAAGC AGGCTAAATT AGTGGAGCAA AAGAAAAAAG AAAGCTTGGC GTTTAAAAGC	900						
	GAAGTGGAAA ACGCCAAAAA CAAAACGCGC CACCTGGCCC TAAAACTCCT TAAAAAATTA	960 1020						
-	GAAACCTTGC AAAAAAACCT GGAATCGATC AATAAAATCA TCAAACAGAA TGAAAAAATC	1020						
10	GCGCAAATTT ATGCGCTTGA TTTGAAAACT AATGGCGATT ACAACGCTTA TTACAACGCC	1140						
-	TTGAATGACA AAATCACTAT TCAAATCACC CAGCTTGAAA CCTTAAGCGC TCTAAATAGT	1200						
	GCTTATTTGT CCTTACAAAA TCTCAAAGGA TTAGAATGA	1239						
**								
1.5	(2) INFORMATION FOR SEQ ID NO:52:							
15	(i) CROUDINGE CHADACHERICATION							
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 414 base pairs							
	(B) TYPE: nucleic acid							
	(C) STRANDEDNESS: double							
20	(D) TOPOLOGY: circular							
-	(ii) MOLECULE TYPE: DNA (genomic)							
	(1111) THEORETICAL AND							
25	(iii) HYPOTHETICAL: NO							
23	(iv) ANTI-SENSE: NO							
	(21) 12:12 52:152. 110							
	(vi) ORIGINAL SOURCE:							
	(A) ORGANISM: Helicobacter pylori							
30								
	(ix) FEATURE:							
	(A) NAME/KEY: misc_feature (B) LOCATION 1414							
	(b) LOCATION 1414							
35	(xi) SEQUENCE DESCRIPTION: SEO ID NO:52:							
	• • • • • • • • • • • • • • • • • • • •							
	ATGCGTATAG TTAGAAATTT ATTTCTTGTA TCGTTTGTGG CGTATAGTAG TGCGTTCGCA	60						
	GCGGATTTAG AAACCGGAAC CAAAAACGAC AAAAAGAGCG GTAAAAAATT TTACAAACTC	120						
40	CATAAAAACC ATGGCTCAGA AACCGAGACT AAAAACGATA AAAAGCTTTA TGATTTCACT	180						
40	AAAAATAGCG GATTAGAAGG CGTGGATTTA GAAAAAAGCC CTAACCTTAA AAGCCATAAA	240						
	AAAAGCGATA AAAAGTTTTA TAAACAACTC GCTAAAAACA ATATCGCTGA AGGGGTGAGC ATGCCGATTG TGAATTTCAA TAAAGCCCTA TCTTTTGGGC CTTATTTTGA AAGGACTAAA	300						
	AGCAAAAAA CCCAATACAT GGACGGCGG TTGATGATGC ACATCCGTTT TTAA	360 414						
		47.ż						
45	(2) INFORMATION FOR SEQ ID NO:53:							
	(i) SEQUENCE CHARACTERISTICS:							
	(A) LENGTH: 930 base pairs	,						
50	(B) TYPE: nucleic acid							
50	(C) STRANDEDNESS: double (D) TOPOLOGY: circular							
	(D) TOPOLOGI: CITCUIAL							
•	(ii) MOLECULE TYPE: DNA (genomic)							
55	(iii) HYPOTHETICAL: NO							

```
(iv) ANTI-SENSE: NO
        (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...930
10
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:
     TTGATGCCAC AAAACCAGCT TGTGATCACC ATCATTGATG AATCAGGCTC TAAGCAACTC
     AAATTTTCTA AAAATTTAAA ACGCAACCTC ATCATTCTG TTGTCATTCT TTTATTGATC
15 GTGGGGCTTG GCGTGGGGTT TTTAAAATTT TTAATCGCTA AAATGGATAC GATGACAAGC
     GAGAGGAATG CGGTTTTAAG GGATTTTAGG GGTTTGTATC AAAAAAATTA CGCCCTAGCG
     AAAGAGATTA AAAACAAGCG AGAAGAGCTT TTTATTGTGG GGCAAAAGAT CCGTGGGCTA
                                                                         300
     GAATCCTTGA TTGAAATCAA AAAGGGGGCT AATGGGGGAG GGCATCTCTA TGATGAAGTG
                                                                         360
     GATTTAGAAA ATTTGAGCTT AAATCAAAAA CATTTAGCAC TCATGCTCAT TCCTAATGGC
                                                                         420
     ATGCCCCTAA AAACTTATAG CGCTATCAAA CCCACTAAAG AAAGGAACCA CCCCATTAAA
                                                                         480
     AAGATTAAGG GCGTTGAATC CGGGATCGAT TTTATCGCGC CATTGAACAC GCCTGTGTAT
     GCGAGCGCTG ATGGGATTGT GGATTTTGTG AAGACTCGTT CTAATGCGGG GTATGGGAAC
     TTGGTGCGCA TTGAACATGC GTTTGGTTTC AGCTCCATTT ATACGCACTT AGATCATGTC
     AATGTGCAGC CTAAAAGCTT CATCCAAAAA GGGCAGTTGA TTGGCTATAG CGGGAAGAGC
     GGTAATAGCG GCGGCGAAAA ATTGCATTAT GAAGTGCGGT TTTTGGGTAA AATTTTAGAC
     GCAGAAAAAT TCCTAGCATG GGATTTGGAT CATTTTCAAA GCGCTTTAGA AGAAAATAAA
     TTTATTGAAT GGAAGAATCT GTTTTGGGTT TTAGAAGACA TCGTCCAGCT CCAAGAGCAT
    GTGGATAAAG ACACCTTAAA AGGTCAGTAG
30
   (2) INFORMATION FOR SEQ ID NO:54:
         (i) SEQUENCE CHARACTERISTICS:
              (A) LENGTH: 999 base pairs
              (B) TYPE: nucleic acid
35
              (C) STRANDEDNESS: double
              (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
40
        (iii) HYPOTHETICAL: NO
       (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
45
             (A) ORGANISM: Helicobacter pylori
        (ix) FEATURE:
              (A) NAME/KEY: misc feature
              (B) LOCATION 1...999
50
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:
    GTGCTATATT TTTTAACCAG TTTATTTATT TGCTCTTTGA TTGTTTTGTG GTCTAAAAAA
    TCCATGCTCT TTGTGGATAA CGCTAATAAA ATCCAAGGCT TCCATCATGC AAGAACCCCA
    CGAGCCGGGG GGCTTGGGAT CTTTCTTTCT TTTGCGTTGG CTTGTTATCT TGAACCTTTT
```

```
GAGATGCCTT TTAAGGGGCC TTTTGTTTTC TTAGGGCTAT CGCTAGTGTT TTTGAGCGGT
                                                                          240
     TTTTTAGAAG ACATTAACCT TTCATTAAGC CCCAAAATAC GCCTTATTTT GCAAGCTGTA
                                                                          300
     GGGGTCGTTT GCATCATTTC ATCAACGCCT TTAGTGGTGA GCGATTTTTC GCCCCTTTTT
     AGCTTGCCTT ATTTCATCGC TTTTTTATTC GCTATTTTTA TGCTGGTGGG TATCAGTAAC
     GCTATTAATA TCATTGACGG GTTTAACGGG CTTGCATCTG GGATTTGCGC GATCGCGCTT
     TTAGTCATTC ATTATATAGA CCCTAGCAGT TTGTCTTGTT TGCTCGCTTA CATGGTGCTT
     GGGTTTATGG TGTTAAATTT CCCTTCAGGA AAGATTTTTT TAGGCGATGG GGGGGCGTAT
     TTTTTGGGTT TGGTGTGCGG GATTTCTCTC TTGCATTTGA GTTTGGAGCA AAAAATCAGC
                                                                          660
     GTGTTTTTTG GGCTCAATTT AATGCTTTAT CCGGTCATAG AGGTGCTTTT TAGTATCCTT
                                                                          720
     AGGCGCAAAA TAAAACGCCA GAAAGCCACC ATGCCGGATA ATTTGCATTT GCACACCCTT
                                                                          780
     TTATTTAAAT TCTTGCAACA ACGCTCTTTC AATTACCCTA ACCCTTTATG CGCGTTTATC
     CTTATTCTAT GCAACCTGCC TTTTATTTTA ATAAGCGTTT TGTTTCGCTT GGACGCTTAT
     GCGCTCATTG TGATTAGCCT AGTCTTTATC GCATGCTATT TAATAGGCTA TGCTTATTTG
                                                                          960
     AATAGGCAAG TTTGCGCTTT AGAAAAGCGG GCGTTTTAA
                                                                          999
15
     (2) INFORMATION FOR SEQ ID NO:55:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 816 base pairs
20
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
25
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
30
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
35
               (B) LOCATION 1...816
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:
    ATGAACATAT TCAAGCGTAT TATTTGCGTA ACCGCTATTG TTTTAGGTTT TTTTAACCTT
    TTAGACGCCA AACACCACAA AGAAAAAAA GAAGACCACA AAATCACTCG TGAGCTTAAA
                                                                         120
    GTGGGCGCTA ACCCTGTGCC GCATGCGCAA ATCTTGCAAT CAGTTGTGGA TGATTTGAAA
                                                                         180
    GAGAAAGGGA TCAAATTAGT GATCGTGTCT TTTACGGATT ATGTGTTGCC TAATTTAGCG
                                                                         240
    CTCAATGACG GCTCTTTAGA CGCGAATTAC TTCCAGCACC GCCCTTATTT GGATCGGTTT
                                                                         300
    AATTTGGACA GAAAAATGCA CCTTGTTGGT TTGGCCAATA TCCATGTGGA GCCTTTAAGA
    TTTTATTCTC AAAAAATCAC AGACATTAAA AACCTTAAAA AAGGCTCAGT GATTGCTGTG 420
    CCAAATGATC CGGCCAATCA AGGCAGGGCG TTGATTTTAC TCCATAAACA AGGCCTTATC
                                                                         480
    GCTCTCAAAG ACCCAAGCAA TCTATACGCT ACGGAGTTTG ATATTGTCAA AAATCCTTAC
                                                                         540
    AACATCAAAA TCAAACCCCT AGAAGCTGCG TTATTGCCTA AGGTTTTAGG GGATGTGGAT
                                                                         600
    GGGGCTATCA TAACAGGGAA TTATGCCTTG CAAGCAAAAC TCACCGGAGC CTTATTTTCA
                                                                         660
    GAAGATAAGG ACTCGCCTTA TGCTAATCTT GTAGCCTCTC GTGAGGATAA TGCGCAAGAT
50
                                                                         720
    GAAGCGATAA AAGCGTTGAT TGAAGCCTTA CAGAGCGAAA AGACCAGGAA ATTCATTTTG
                                                                         780
    GATACCTATA AGGGGGCGAT TATCCCGGCT TTTTAA
```

(2) INFORMATION FOR SEQ ID NO:56:

```
(i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 951 base pairs
                (B) TYPE: nucleic acid
                (C) STRANDEDNESS: double
                (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
         (iii) HYPOTHETICAL: NO
10
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
                (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
                (B) LOCATION 1...951
20
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:
     ATGCAAGAAT TCAGTTTGTG GTGCGATTTT ATAGAAAGGG ATTTTTTAGA AAACGATTTT
     TTAAAGCTCA TCAATAAGGG GGCTATTTGC GGGGCGACGA GTAACCCTAG TTTGTTTTGC
     GAAGCGATCA CAAAAAGCGC GTTTTATCAA GATGAAATCG CTAAACTCAA AGGCAAAAAA
     GCTAAAGAAA TTTATGAAAC TCTGGCACTA AAGGATATTT TACAAGCCTC TAGCGCGTTA
     ATGCCTTTGT ATGAAAAAGA CCCTAACAAC GGCTACATCA GCCTAGAAAT TGACCCCTTT
     TTAGAAGACG ATGCGATTAA AAGCATTGAT GAAGCCAAGC GGTTATTCAA AACATTAAAC
     CGCCCCAATG TGATGATTAA AGTCCCGGCG AGTGAAAGCG CTTTTGAAGT CATTAGCGCT
     CTGGCTCAAG CCTCTATCCC CATTAATGTA ACTTTAGTCT TTTCGCCTAA AATTGCCGGT
     GAAATCGCTC AAATCTTAGC CAAAGAAGCA CGAAAAAGAG CGGTCATTAG CGTGTTTGTC
     TCACGATTTG ACAAAGAAAT AGACCCACTA GTGCCACAAA ATTTGCAAGC TCAAAGTGGG
     ATCATGAACG CTACCGAGTG TTATTATCAA ATCAACCAGC ATGCTAATAA GCTAATAAGC
     ACCCTTTTTG CATCCACCGG CGTTAAATCT AATTCTTTAG CTAAAGATTA CTACATTAAA
     GCGCTGTGTT TTAAAAACTC TATCAACACA GCCCCCTAG ACGCCCTAAA CGCTTATTTG
                                                                         780
     CTTGACCCAA ACACCGAGTG TCAAACCCCT TTAAAAATCA CAGAAATTGA AGCGTTCAAA
                                                                         840
     AAAGAATTAA AAACGCACAA TATTGATTTA GAAAACACCG CCCAAAAACT CCTTAAAGAA
                                                                         900
     GGCTTGATAG CGTTCAAACA ATCCTTTGAA AAGCTTTTAA GCAGTTTTTG A
                                                                         951
     (2) INFORMATION FOR SEQ ID NO:57:
40
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 783 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
45
               (D) TOPOLOGY: circular
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
50
         (iv) ANTI-SENSE: NO
```

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

660

55

(ix) FEATURE:

- 131 -

	(A) NAME/KEY: misc_feature (B) LOCATION 1783	
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:	
		<b></b>
	ATGAAAACAA ATGGTCATTT TAAGGATTTT GCATGGAAAA AATGCTTTTT AGGCGCGAGC	60
	GTGGTGGCTT TATTAGTGGG GTGTAGCCCG CATATTATTG AAACCAATGA AGTTGCTTTG	120
10	AAATTGAATT ACCATCCAGC TAGCGAGAAA GTTCAAGCGT TAGATGAAAA GATTTTACTT	180
10	TTAAGGCCAG CTTTCCAATA CAGCGATAAT ATTGCTAAAG AGTATGAAAA CAAATTCAAG	240
	AATCAAACCA CGCTTAAAGT TGAAGAGATC TTGCAAAATC AGGGCTATAA GGTTATTAAT GTGGATAGCA GCGATAAAGA CGATTTTTCT TTTGCGCAAA AAAAAGAAGG GTATTTGGCT	300 360
	GTGGATAGCA GCGATAAAGA CGATTTTTCT TTTGCGCAAA AAAAAGAAGG GTATTTGGCT GTCGCTATGA ATGGCGAAAT TGTTTTACGC CCCGATCCTA AAAGGACCAT ACAGAAAAAA	420
	TCAGAACCCG GGTTATTATT CTCCACTGGT TTGGATAAAA TGGAAAGGGT TTTAATCCCG	480
1.5	GCTGGGTTTG TCAAGGTTAC CATACTAGAG CCTATGAGTG GGGAATCTTT GGATTCTTTT	540
15	ACGATGGATT TGAGCGAGTT GGACATCCAA GAAAAATTCT TAAAAACCAC CCATTCAAGC	600
	CATAGOGGAG GGTTAGTTAG CACTATGGTT AAGGGGACGG ATAATTCTAA TGACGCAATT	660
	AAGAGCGCTT TGAATAAGAT TTTTGCAAGT ATCATGCAAG AAATGGATAA GAAACTCACT	720
	CAAAGGAATT TAGAATCTTA TCAAAAAGAC GCCAAGGAAT TAAAAAACAA GAGAAACCGA	780
20	·	783
20	TAA	,05
	(2) INFORMATION FOR SEQ ID NO:58:	
	(2) INIONALION FOR DDG 12 NO.301	
	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 4149 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	·	
30	(ii) MOLECULE TYPE: DNA (genomic)	
	/ · · · · · · · · · · · · · · · · · · ·	,
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
35	(IV) MIII DEMODE. NO	
-	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
40	(A) NAME/KEY: misc_feature	
	(B) LOCATION 14149	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:	
		_
45	TTGAATTTTA ATAACCTTAC GGCTAATGGG GCGTTAAATT TTAATGGTTA TGCGCCCTCT	60
	TTAACTAAGG CTTTAATGAA TGTCAGCGGG CAGTTTGTTT TAGGGAATAA TGGGGATATT	120
	AATTTATCTG ACATCAATAT CTTTGACAAC ATCACAAAAT CTGTAACTTA CAACATCTTA	180
	AACGCTCAAA AAGGGATTAC TGGCATTAGT GGGGCTAATG GCTATGAAAA AATCCTTTTT	240
	TATGGCATGA AAATCCAAAA CGCTACCTAT AGCGATAATA ACAACATCCA AACTTGGTCG	300
50	TITATAAACC CTCTCAATTC TTCTCAAATC ATTCAAGAGA GCATTAAAAA TGGGGATCTA	360
	ACCATAGAAG TTTTAAATAA CCCTAACTCG GCTTCCAACA CTATTTTTAA TATCGCTCCT	420
	GAGCTTTATA ATTACCAAGA TTCTAAGCAA AATCCTACCG GCTATAGCTA TGATTATAGC	480
	GACAATCAAG CAGGCACTTA TTACTTGACA AGCAACATTA AAGGTCTTTT CACCCCTAAA	540

GGCTCTCAAA CGCCTCAAAC CCCAGGCACT TATAGCCCAT TTAACCAGCC TTTGAATAGT

TTGAATATCT ACAATAAGGG TTTTTCTAGC GAGAATTTAA AAACGCTTTT AGGGATCCTT

	•						
	TCTCAAAATT	CCGCCACCTT	AAAAGAAATG	ATTGAATCCA	ACCAACTAGA	CAATATCACT	720
	AACATTAATG	AAGTGTTGCA	ACTCTTAGAT	AAGATTAAAA	TCACCCAAGO	GCAAAAGCAA	780
	GCGCTCCTAG	AAACGATCAA	CCATTTGACT	GACAACATCA	ATCAAACCTT	TAATAACGGG	840
	AATCTCGTTA	TAGGCGCTAC	CCAAGATAAT	GTTACAAACT	CTACTAGCTC	TATATGGTTT	900
5	GGGGGCAATG	GCTATAGCAG	CCCTTGCGCG	CTAGATAGCG	CCACTTGTTC	TTCTTTTAGA	960
	AACACTTACT	'TGGGGCAATT	ATTAGGCTCA	ACTTCCCCTT	ATTTAGGCTA	CATTAACGCT	1020
	GATTTTAAAG	CTAAAAGCAT	TTATATTACC	GGGACAATTG	GAAGTAGTAA	CGCTTTTGAA	1080
	AGCGGAGGGA	GCGCGGATGT	AACCTTTCAA	AGCGCTAATA	ACTTAGTGTT	GAATAAAGCT	1140
	AACATAGAAG	CTCAAGCCAC	AGACAATATC	TTTAATCTTT	TGGGTCAAGA	AGGGATTGAT	1200
10	AAAATCTTTA	ATCAGGGGAA	TTTAGCGAAT	GTTCTTAGTC	AAATGGCTAT	GGAAAAATC	1260
	AAGCAAGCCG	GCGGTTTAGG	GAACTTTATA	GAAAACGCTC	TAAGCCCTTT	GAGTAAGGAA	1320
• 6	TTACCCGCTA	GCTTGCAAGA	TGAAACCTTA	GGCCAACTTA	TAGGTCAAAA	TAACTTAGAT	1380
	GATTTATTGA	ATAATAGTGG	AGTCATGAAT	GAAATCCAAA	ACATTATCAG	ТСАВАВАСТА	1440
	AGCATTTTTG	GCAATTTTGT	TACCCCATCC	ATCATAGAAA	ACTACCTTGC	TAAGCAGTCT	1500
15	TTAAAAAGCA	TGCTAGACGA	TAAAGGGCTT	TTGAATTTTA	TCGGTGGGTA	TATAGACGCT	1560
	TCTGAATTAA	GCTCTATTTT	AGGCGTGATT	TTAAAGGATA	TTACTAACCC	CCCTACAAGC	1620
	CTGCAAAAAG	ACATTGGTGT	GGTAGCGAAC	GACTTGTTGA	ACGAGTTTTT	AGGACAAGAT	1680
	GTTGTCAAAA	AGCTAGAAAG	TCAAGGCTTG	GTGAGTAATA	TCATCAATAA	TGTTATTTCT	1740
	CAAGGCGGGT	TGAGCGGCGT	TTATAATCAA	GGTTTAGGGA	GCGTGTTGCC	GCCCTCTTTA	1800
20	CAAAACGCGC	TCAAAGAAAA	CGATTTAGGC	ACTCTTTTAT	CGCCTAGAGG	CTTGCATGAT	1860
	TTTTGGCAAA	AAGGGTATTT	TAACTTTTTA	AGCAATGGCT	ATGTTTTTGT	CAATAACAGC	1920
	TCTTTTAGTA	ACGCTACTGG	GGGTAGTTTG	AATTTTGTCG	CCAACAAGTC	TATTATCTTT	1980
	AATGGCGATA	ATACGATTGA	CTTTAGCAAG	TATCAAGGCG	CATTGATTTT	TGCTTCTAAT	2040
_	GGTGTTTCTA	ATATCAATAT	CACCACCCTA	AACGCCACTA	ATGGCTTAAG	CCTTAATGCG	2100
25	GGTTTGAATA	ATGTGAGCGT	TCAAAAAGGA	GAAATTTGTA	TCAATTTAGC	CAATTGCCCT	2160
	ACAACCAAAA	ACAGCTCTCC	TGCAAACTCT	AGCGTAACCC	CCACTAATGA	GTCTTTAAGC	2220
	GTGCACGCTA	ATAATTTCAC	TTTCTTAGGC	ACAATCATCT	CTAATGGGGC	TATTGATTG	2280
	TCTCAAGTAA	CAAATAATAG	CGTTATAGGC	ACGCTCAATC	TCAATGAAAA	TGCGACCTTG	2340
	CAAGCTAATA	ATTTAACGAT	CACCAACGCT	TTTAACAACG	CCTCTAACTC	TACGGCTAAT	2400
30	ATTGATGGTA	ATTTCACCTT	AAACCAACAA	GCGACTTTAA	GCACTAACGC	TAGTGGTTTG	2460
	AATGTCATGG	GGAATTTTAA	TAGCTATGGC	GATTTGGTGT	TTAACCTCAG	TCATTCAGTT	2520
	AGTCATGCTA	TTATCAATAC	TCAAGGCACA	GCGACGATCA	TGGCCAATAA	TAACCCTTTC	2580
•	ATCCAATTCA	ACGCTTCTTC	AAAAGAAGTG	GGTACTTACA	CGCTGATTGA	TAGCGCTAAA	2640
	GCCATTTATT	ACGGGTATAA	CAACCAAATC	ACAGGAGGCA	GTAGCCTGGA	ТАВТТАССТТ	2700
35	AAGCTTTATG	CGCTCATTGA	TATTAATGGC	AAGCACATGG	TGATGACTGA	CAACGGCTTA	2760
	ACCTATAACG	GGCAAGCCGT	GAGCGTTAAA	GATGGCGGTT	TAGTTGTAGG	CTTTDAGGAC	2820
	TCTCAAAATC	AATACATTTA	CACTTCCATT	CTTTATAATA	AAGTGAAAAT	CCCTCTTTCT	2880
	AATGATCCTA	TCAATAACCC	ACAAGCCCCC	ACTTTAAAAC	AATATATCCC	TCAAATTCAG	2940
	GGCGTTCAAA	GCGTGGATAG	CATCGATCAA	GCTGGGGGAA	ATCAAGCGAT	TAATTCCCTC	3000
40	AATAAAATCT	TTGAAACTAA	AGGAAGCCCT	TTATTCGCTC	CCTATTATCT	AGAGAGCCAC	3060
	TCCACAAAAG	ATTTAACCAC	GATCGCTGGA	GATATTGCTA	ACACTTTAGA	ACTCATCCCT	3120
	AACCCTAATT	TTAAAAATGA	CGCCACTAAT	ATTTTACAGA	TCAACACCTA	CACGCAGCAA	3180
	ATGAGTCGTT	TAGCCAAGCT	CTCTGACACT	TCAACTTTCG	CCCGTTCTGA	THEOCHEROCAL	3240
	CGCTTAGAAG	CCCTTAAAAA	CAAGCGATTC	GCTGATGCGA	TCCCTAACGC	TATECATETE	3300
45	ATTTTAAAAT	ACTCTCAAAG	GAATAGAGTT	AAAAATAATG	TCTCCCCCAC	ACCACTUCCA	3360
	GGGGCTAGTT	TCATTAGTGG	AGGTACTGGA	ACTTTATATG	GTATCAATGT	ACCCTATCAT	3420
	AGGTTTATTA	AGGGCGTGAT	TGTGGGAGGT	TATGCCGCTT	ATGGGTATAG	CCCCTTCCAT	3480
•	GCAAACATCA	CTCAATCAGG	CTCTAGCAAT	GTCAATGTGG	GCGTTTATAG	CCGACCCTTT	3540
	ATCAAAAGAA	GCGAGCTAAC	CATGAGCTTG	AATGAGACTT	GGGGATACAA	TAAAGCGIII	3600
50	ATCAACTCCT	ATGACCCCCT	ACTCTCAATC	ATCAATCAGT	CTTDCACACAC	CCVCVCTTTC	3660
	ACGACTGACG	CTAAAATCAA	TTATGGCTAT	GATTTCATCT	TTADAGATA	V V C C C C C C C C C C C C C C C C C C	•
	TTTAAACCCC	AAGTAGGCTT	AAGCTATTAT	TACATTGGTT	åCahCahGGabana ÷ + caeseseses terμ	VACCCCCAME	3720
	ATGGATGATC	CTATTTACAA	CCAATTCAGA	GCCAATGCTG	TOTOTOGITI	AAAATCCCTTT	3780
	CTAACGATCA	ATTTTGCCCT	AGAAAGTCGC	CATTATTTCA	THAT A A A COURT	THE THE PROPERTY OF THE PROPER	3840
55	GTGATTGCGG	ATGTGGGCAG	AGACTTATTC	ATTAATTCTA	TGGGGGDTN N	YATCOTOCO	3900
					TOGGGGHIWA	ANTOGIGCGI.	3960

WO 98/18323 PCT/US97/19575

- 133 -

TTCATCGGTA ATAACACCCT AAGCTATAGA GATGGTGGCA ATTATCACAG GCGGGGAGAT AAGATTGTTC AAAACCTTTT GCTAGGTTTG GGCTTGATTA TAAAGATATT AATATTACCG GCTTTTTAA	ATGTGAATGC	GGGCATAGGG	4020 4080 4140 4149
(2) INFORMATION FOR SEQ ID NO:59:			. '
(2) INFORMATION FOR SEQ ID NO:55:			
<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 789 base pairs</li><li>(B) TYPE: nucleic acid</li></ul>			
(C) STRANDEDNESS: double			•
(D) TOPOLOGY: circular			•
(ii) MOLECULE TYPE: DNA (genomic)			
(iii) HYPOTHETICAL: NO			
(III) MITOMETERS NO	•		
(iv) ANTI-SENSE: NO			
(vi) ORIGINAL SOURCE:		•	
(A) ORGANISM: Helicobacter pylori	-	·	
(ix) FEATURE:			
(A) NAME/KEY: misc_feature (B) LOCATION 1789			
(B) LOCATION 1/83			
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59			
ATGAAAAAA TTGGTTTGAG CTTGTGTTTG GTTTTGAGTT	TGGGTTTTTT	AAAAGCCCAT	60
GAAGTGAGCG CTGAAGAGAT TGCGGATATT TTCTACAAAC	TCAACGCCAA	AGAGCCTAAA	120
ATGAAAATCA ACCACACGAA GGGGTTTTGC GCTAAAGGCG			180
GCAAGAGAGG ATTTAGAGGT GCCACTACTC AATGAAAAAG			240
TATTCTTTAG GGGGCGTGGC GATGGACGAT AAAAGCAAGG			300
CTAGAAAATC AAAACGCTAG TTGGACAATG GTGATGCTCA AAAAACCCTG AAGAATTCGC CCAATTTTTT GAAATGAGAC			360 420
GATGAAGCAA GAATCAAAAA GCTTTACGAA GAAGTCCCCT			480
TATATGAAAA CGATAGGGAT TAGCTCAAGC GTGGCTAATA			540
GCGTTCAAGT TTAAAGATAA GAAAGAAAAA TTATTGCCTG			600
AAAGAGGGCG TTAAATACTT AAATCCTCAA GAATTAAAGC			660
CTCTCTTCAT TCCAACAACA CCTTAAAAAT AAACCCATAG	AATACCAAAT	GTATTTGGTG	720
TTTGCGAATC AAAATGATGC CACCAACGAC ACGACCGCGC	TTTGGAAAGG	CAGCATAAGG	780
AATTATTAG			789
	•	•	
(2) INFORMATION FOR SEQ ID NO:60:			
(i) SEQUENCE CHARACTERISTICS:		,	
(A) LENGTH: 741 base pairs			
(B) TYPE: nucleic acid			
(C) STRANDEDNESS: double			
(D) TOPOLOGY: circular			
(ii) MOLECULE TYPE: DNA (genomic)			

(iii) HYPOTHETICAL: NO

	(iv) ANTI-SENSE: NO	
	( ))	
	(vi) ORIGINAL SOURCE:	
5	(A) ORGANISM: Helicobacter pylori	
,	(ix) FEATURE:	
•	(A) NAME/KEY: misc feature	٠.
:	(B) LOCATION 1741	
	(L)	
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:	
	ATGAAACAAT TTAAAAAGAA ACCAAAAAAG ATAAAACGAT CGCATCAAAA TCAAAAAACA	60
·	ATCTTAAAGC GTCCTTTATG GCTTATGCCT TTACTGATTG GCGGGTTTGC TAGTGGGGTG	120
	TATGCGGATG GAACAGACAT TTTGGGGCTT AGTTGGGGGG AAAAAAGCCA AAAGGTATGC	180
15	GTGCATCGTC CATGGTATGC TATATGGAGT TGCGATAAAT GGGAGGAAAA AACACAACAA	240
	TTTACAGGAA ACCAACTCAT CACAAAAACT TGGGCAGGGG GTAATGCGGC TAACTACTAC	300
	CACTCTCAAA ACAACCAAGA CATCACAGCC AATTTAAAAA ATGATAACGG CACTTATTTT	360
	TTAAGCGGTC TGTATAACTA CACCGGAGGG GAATATAATG GGGGGAATTT AGACATTGAA	420
	TTAGGCAGTA ACGCTACTTT TAATCTAGGT GCGAGTAGTG GGAATAGCTT CACTTCTTGG	480
20	TATCCTAATG GGCATACTGA TGTTACTTTT AGCGCTGGGA CTATCAATGT GAATAACAGC	540
	GTAGAAGTGG GCAATCGTGT GGGATCGGGA GCTGGCACGC ACACCGGCAC AGCCACTTTA	600
	AACTTGAACG CTAATAAGGT TACTATCAAT TCCAATATCA GCGCGTATAA AACTTCGCAA	660
	GTGAATGTAG GCAATGCTAA CAGCGTTATT ACCATTAATT CGGTTTCTTT AAATGGGGAA	720
	TACTTGCAGT TCTTTAGCTA G	741
25		
	(2) INFORMATION FOR SEQ ID NO:61:	
	(') GROVENIAR CHIARACHURI CONTAG	
	(i) SEQUENCE CHARACTERISTICS:	
30	(A) LENGTH: 738 base pairs (B) TYPE: nucleic acid	
30	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
	(b) Toronogi. Circular	
	(ii) MOLECULE TYPE: DNA (genomic)	
35		
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
		•
40	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
•	(ix) FEATURE:	
	(A) NAME/KEY: misc_feature	
<b>45</b>	(B) LOCATION 1738	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:	
50	ATGATAAAAA AGACCCTTGC ATCGGTTTTA TTAGGATTGA GTTTGATGAG TGTGTTAAAT	60
20	GCCAAAGAAT GCGTTTCGCC CATAACAAGA AGCGTTAAGT ATCATCAGCA AAGTGCTGAG ATCAGAGCCT TGCAATTACA AAGTTACAAA ATGGCGAAAA TGGCGCTAGA CAATAACCTT	120
	AAGCTCGTTA AAGACAAAAA GCCAGCCGTC ATCTTGGATT TAGATGAAAC CGTTTTGAAC	180 240
	ACTITIGATE ATGCGGGCTA TITAGTCAAA AACTGCATTA AATACACCCC AGAAACTTGG	300
	GATAAATTIG AAAAAGAAGG CTCTCTTACG CTCATTCCTG GAGCGCTAGA CTTTTTAGAA	360
55	f 10	420

5	GCTAAAAACA GCCAAGAACA ACAAGCCAAA GTCTTGCAAA ACGCTCAAAA ATTCGGCACA GAATGGATCA TTTTACCCAA CTCTCTTTAT GGCACATGGG AAGATGGGCC TATAAAAGCA TGGCAAAATA AAAAATAA  (2) INFORMATION FOR SEQ ID NO:62:  (1) SEQUENCE CHARACTERISTICS:	660 720 738
		•
	(i) SEQUENCE CHARACTERISTICS:	
10	<ul><li>(A) LENGTH: 867 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li><li>(D) TOPOLOGY: circular</li></ul>	
15	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
20	(iv) ANTI-SENSE: NO	
	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
25	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1867</pre>	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:	
	TTGTGGTGTT TAAAAACCCC TATCATAGGG CATGGCATGA AGAAAAAGC AAAAGTCTTT TGGTGTTGTT TTAAAATGAT TCGTTGGTTG TATTTGGCGG TCTTTTTTTT GTTGAGCGTA TCAGACGCTA AAGAAATCGC TATGCAACGA TTTGACAAAC AAAACCATAA GATTTTTGAA ATCCTTGCGG ATAAAGTGAG CGCCAAAGAC AATGTGATAA CCGCCTCAGG GAATGCGATC	60 120 180 240
35	CTATTGAATT ATGACGTGTA TATTCTAGCG GATAAGGTGC GTTATGACAC CAAGACTAAA GAAGCGTTAT TAGAAGGCAA TATTAAGGTT TATAGGGGCG AGGGCTTGCT CGTTAAAACC GATTATGTGA AATTGAGTTT GAACGAAAAA TATGAGATCA TTTTCCCCTT TTATGTCCAA GACAGCGTGA GCGGGATTTG GGTGAGCGC GATATTGCTA GCGGGAAGGA TCAAAAATAT	300 360 420 480
40	AAGATTAAAA ACATGAGCGC TTCAGGGTGC AGCATTGACA ACCCCATTTG GCATGTCAAT GCGACTTCAG GCTCATTTAA CATGCAAAAA TCGCATTTGT CAATGTGGAA TCCTAAGATT TATGTCGGCG ATATTCCTGT ATTGTATTTG CCCTATATTT TCATGTCCAC GAGCAATAAA AGAACTACCG GGTTTTTATA CCCTGAGTTT GGCACTTCCA ACTTAGACGG CTTTATTTAT	540 600 660 720
	TTGCAACCCT TTTATTTAGC CCCCAAAAAC TCATGGGATA TGACCTTTAC CCCACAAATC CGTTACAAAA GGGGTTTTGG CTTGAATTTT GAAGCGCGCT ACATCAACTC TAAGACGCAG GTTTTTATTC AATGCGCGCT ATTTTAG	780 840 867
	(2) INFORMATION FOR SEQ ID NO:63:	•
50	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 387 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

```
(iv) ANTI-SENSE: NO
 5
          (vi) ORIGINAL SOURCE:
                (A) ORGANISM: Helicobacter pylori
          (ix) FEATURE:
10
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...387
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:
15
     TTGATGTTTA AAAAAATGTG TTTGAGCCTG CTAATGATAA GCGGTGTTTG TGTGGGGGCA
                                                                           60
     AAGGATTTGG ATTTCAAGCT GGATTATCGC GCGACTGGGG GGAAATTCAT GGGGAAAATG
                                                                          120
     ACGGACTCTA GTCTTTTAAG TATCACTTCT ATGAACGATG AACCGGTGGT GATTAAAAAC
     CTTATTGTCA ATAGGGGAAA TTCATGCGAA GCGACTAAAA AAGTAGAACC CAAATTTGGC
     GATAAGTTTA AAAAAGAAAA ACTCTTTGAT CATGAATTAA AATACTCGCA ACAGATATTT
     TACCGCCTGG ATTGCAAGCC TAACCAATTG TTAGAAGTTA AAATCATCAC GGACAAGGGC
                                                                          360
     GAATATTACC ATAAATTTTC CAAATAG
                                                                          387
     (2) INFORMATION FOR SEQ ID NO:64:
25
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 510 base pairs
               (B) TYPE: nucleic acid
               (C) STRANDEDNESS: double
               (D) TOPOLOGY: circular
30
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
35
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
40
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...510
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:
45
     ATGCAAGCGT TAAAATCATT GCTTGAAGTG ATTACAAAAC TCCAGAATCT AGGCGGCTAT
    TTGATGCATA TAGCTATTTT CATCATTTTT ATTTGGATTG GAGGGCTTAA GTTTGTGCCT
     TACGAAGCTG AAGGGATCGC CCCTTTTGTG GCCAACTCCC CTTTCTTTTC TTTCATGTAT
                                                                         180
    AAATTTGAAA AACCTGCATA CAAACAACAC AAAATGTCTG AATCCCAATC CATGCAAGAA
                                                                         240
    GAAATGCAAG ATAACCCTAA AATCGTTGAA AACAAAGAAT GGCATAAAGA AAACCGCACT
                                                                         300
    TATTTAGTGG CTGAAGGTTT AGGGATTACG ATCATGATCC TAGGCATTTT GGTGCTTTTG
                                                                         360
    GGGCTTTGGA TGCCTTTAAT GGGCGTAGTT GGGGGCTTGC TTGTCGCTGG AATGACGATC
    ACCACCCTAT TCTTTTTAT TCACAACGCC AGAAGTGTTT GTCAATCAGC ATTTCCCATG
                                                                         480
    GCTTTCTGGG GCTGGAAGGC TAGTGGTTAA
                                                                         510
55
```

- 137 -

## (2) INFORMATION FOR SEQ ID NO:65:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1464 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: circular
- (ii) MOLECULE TYPE: DNA (genomic)

10 (iii) HYPOTHETICAL: NO

- (iv) ANTI-SENSE: NO
- - (ix) FEATURE:
    - (A) NAME/KEY: misc\_feature
- 20 (B) LOCATION 1...1464
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

	ATGATTGAAT	GGATGCAAAA	TCATAGAAAG	TATTTAGTGG	TTACGATATG	GATAAGCACG	60
25	ATCGCTTTTA	TTGCCGCCGG	AATGATAGGT	TGGGGGCAAT	ACAGCTTTTC	TTTAGATAGC	120
	GATAGCGCTG	CCAAAGTGGG	ACAGATTAAG	ATTTCTCAAG	AAGAATTAGC	CCAAGAATAC	180
	CGCCGCCTTA	AAGACGCCTA	TGCTGAGTCT	ATCCCTGATT	TTAAAGAACT	CACCGAAGAT	240
	CAAATCAAAG	CCATGCATTT	AGAAAAAAGC	GCGCTAGATT	CGCTCATCAA	TCAAGCTTTA	300
	TTGAGGAATT	TCGCTTTAGA	TTTAGGGCTT	GGTGCTACCA	AGCAAGAAGT	GGCCAAAGAG	360
30	ATCAGAAAAA	CGAACGTTTT	TCAAAAAGAT	GGCGTTTTTG	ATGAAGAATT	GTATAAAAAT	420
	ATCTTAAAAC	AAAGCCATTA	CCGCCCCAAG	CATTTTGAAG	AAAGCGTTGA	AAGGCTTTTA	480
	ATCCTTCAAA	AAATCAGCGC	TCTATTCCCC	AAAACCACCA	CCCCTTTGGA	GCAATCCAGT	540
	CTATCGCTTT	GGGCAAAATT	GCAAGACAAA	TTAGACATTC	TTATCCTAAA	TCCTAATGAT	600
	GTTAAAATCT	CTCTCAATGA	AGAAGAGATG	AAAAAATATT	ATGAAAACCA	TAGAAAGGAT	660
35	TTTAAAAAGC	CCACAAGCTT	TAAAACACGC	TCTTTATATT	TTGACGCTAG	TTTAGAAAAA	720
	ACTGATTTGA	AAGAGTTGGA	GGAATACTAC	CATAAAAACA	AGGTGTCTTA	TTTGGACAAA	780
	GAGGGGAAAT	TACAGGATTT	TAAAAGCGTT	CAAGAGCAAG	TCAAGCATGA	TTTAAACATG	840
	CAAAAGGCGA	ATGAAAAAGC	CTTAAGGAGC	TATATCGCTC	TAAAAAAGGG	GAACGCACAA	900
	AACTACACCA	CGCAAGATTT	TGAAAAAAAC	AACTCCCCCT	ATACTGCTGA	AATCACGCAA	960
40	AAACTCACCG	CTCTCAAGCC	CCTTGAAGTC	CTAAAACCAG	AGCCTTTTAA	AGATGGTTTT	1020
	ATCGTGGTGC	AGCTTGTCTC	TCAAATTAAA	GACGAATTGC	AAAATTTTGA	TGAAGCCAAA	1080
	AGCGCTCTTA	AAACCCGTCT	GACTCAAGAA	AAAACCCTTA	TGGCGTTGCA	AACTTTAGCT	1140
•	AAAGAAAAGC	TTAAGGATTT	TAAAGGGAAA	AGCGTGGGTT	ATGTAAGCCC	TAATTTTGGA	1200
	GGCACTATCA	GTGAACTTAA	CCAAGAAGAG	AGCGCGAAGT	TTATCAACAC	CCTTTTTAAC	1260
45	CGCCAGGAAA	AAAAAGGGTT	TGTAACCATA	GGTAATAAAG	TGGTGCTTTA	TCAAATCACA	1320
•	GAGCAAAATT	TCAATCACCC	CTTTAGTGCA	GAAGAAAACC	AATACATGCA	GCGTTTAGTC	1380
•	AATAACACTA	AAACGGATTT	TTTTGATAAA	GCGTTGATAG	AAGAATTGAA	AAAACGCTAT	1440
-	AAGATAGTCA	AATACATTCA	ATAA				1464

- 50 (2) INFORMATION FOR SEQ ID NO:66:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 429 base pairs
    - (B) TYPE: nucleic acid
- 55 (C) STRANDEDNESS: double

	(D) TOPOLOGY: circular			
	(ii) MOLECULE TYPE: DNA (genomic)			
5				
)	(iii) HYPOTHETICAL: NO		•	
•	(iv) ANTI-SENSE: NO			
	(vi) ORIGINAL SOURCE:		٠	
10	(A) ORGANISM: Helicobacter pylori	•		•
	(ix) FEATURE:			
	(A) NAME/KEY: misc_feature	* **		
15	(B) LOCATION 1429			
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66	:		
	ATGAAAACGA ACTTTTATAA AATTAAATTA CTATTTGCTT	GGTGTCTTAT	CATTGGCATG	60
20	TTTAACGCTC CGCTTAACGC TGACCAAAAC ACGGATATAA			120
20	ATGGCGCTAA ATAGCGTGGG GCTTGTTTCT AGAGATCAGC GAAACCCTAG AGCAAAAAGT GGCCATACTC AATGACTATA	TAAAAATAGA	GATCCCTAAA	180 240
	AAGTTTGACG ACATAAGTTT AGGGAGTTTC CAACCTAATG	ATAATCTAGG	TATCAATGCG	300
	ATGTGGGGCA TTCAAAATCT TCTCATGAGC CAAATGATGA			360
25	TCTTTCATGT ATGGCTATGC GCCAACATAC TCAGATTCAT GGGTATTAA	CGTTTTTACC	ACCGATCTTA	420
	(2) INFORMATION FOR SEQ ID NO:67:			
	•			
30	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 627 base pairs			
50	(B) TYPE: nucleic acid			
	(C) STRANDEDNESS: double			
	(D) TOPOLOGY: circular	4		
35	(ii) MOLECULE TYPE: DNA (genomic)			
	(iii) HYPOTHETICAL: NO		•	
	, , , , , , , , , , , , , , , , , , , ,	٠.		
40	(iv) ANTI-SENSE: NO			
40	(vi) ORIGINAL SOURCE:		•	
	(A) ORGANISM: Helicobacter pylori	•		
		٠.		
45	(ix) FEATURE:	•		
<del>-</del> -3	<ul><li>(A) NAME/KEY: misc_feature</li><li>(B) LOCATION 1627</li></ul>	• .		
•				
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67	:		
50	TTGATCAACA ATAATAATAA CAATAAAAAA CTGAGAGGCT			60
	AGTCTCGTTG TTTTCAGTTC GTATGGGTCA GCAAATGACG GCGCTAGAAA AAGAAAAAAA CACTCCCAAT GGGCTTGTTT			120
	AGTTTTAAAG CGACTATCAA AAATTTGAAA GACAAGAAAG			180 240
	CCCGATATTA TCAAAGATGA AGTTTTTGAC TTCGTGATTG			300
55	ATABAGGATT TGAAGCATTA CCATCCACTT ATTGAAAAA	ער באות אורים אינו אינו אינו אינו אינו אינו אינו אינו	י א א א כיכיביים א א	260

	·		the state of the s	
• .	GAAATGGGAT TGAATGTAGA ATTACAGATC AATCCTGAAG AAAAGCATCA GCACGACCAA CAAACAACGC TGCTTTCTAT GAAATTTTAT GCGATGATAA GCTATATAAT GTTTTATTGG CCTAATGATC TTTTGAAACA CATTAGCACC ATAGAGTCTC	CATTGCACGG CCGTATTCAA	AGAAACAAGA TTCTTATGAT	420 480 540 600
5	ATTACATGTG AAGCGGTATA TCTATAA	•	*	627
	(2) INFORMATION FOR SEQ ID NO:68:	•.		
	(i) SEQUENCE CHARACTERISTICS:			
10	(A) LENGTH: 738 base pairs			
	(B) TYPE: nucleic acid	•		
	(C) STRANDEDNESS: double			
	(D) TOPOLOGY: circular			
	•			
15	(ii) MOLECULE TYPE: DNA (genomic)	•		•
	(iii) HYPOTHETICAL: NO			
	(iv) ANTI-SENSE: NO			
20	•	•		
	(vi) ORIGINAL SOURCE:			
	(A) ORGANISM: Helicobacter pylori			
	(ix) FEATURE:			
25	(A) NAME/KEY: misc_feature			
	(B) LOCATION 1738			
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68	:		
30	ATGGCAGGCA CACAAGCTAT ATATGAATCA TCTTCTGCAG	GATTCTTATC	GCAAGTCTCC	60
	TCAATCATCT CAAGCACAAG TGGTGTCGCA GGGCCATTTG	CAGGAATAGT	ÄGCGGGCGCT	120
	ATGACAGCAG CGATTATTCC TATTGTTGTG GGATTTACTA	ATCCGCAAAT	GACCGCTATC	180
	ATGACCCAAT ACAATCAAAG CATCGCTGAA GCTGTAAGCG	TGCCTATGAA	AGCCGCTAAC	240
	CAACAATACA ACCAATTGTA TCAAGGTTTT AACGATCAAA	GCATGGCTGT	GGGGAACAAT	300
35	ATCTTAAATA TCAGCAAATT AACAGGGGAA TTTAACGCGC	AAGGCAACAC	GCAAAGCGCG	360
	CAAATTAGTG CTGTCAATAG TCAGATTGCA AGCATTTTAG	CGAGTAACAC	TACCCCTAAA	420
	AATCCTAGCG CTATTGAAGC TTATGCGACG AATCAAATCG	CTGTTCCTAG	CGTGCCAACA	480
	ACGGTTGAAA TGATGAGCGG TATATTAGGC AATATTACAA	GCGCAGCACC	AAAATACGCC	540
	CTAGCTCTAC AAGAGCAACT GCGTTCTCAA GCAAGCAACA	GCTCAATGAA	TGATACAGCC	600
40	GATTCCCTTG ATAGCTGTAC CGCTTTAGGC GCACTTGTTG	GCTCATCAAA	AGTGTTTTTC	660
	AGTTGCATGC AAATTTCTAT GACTCCTATG AGTGTTTCTA	TGCCCACTGT	TATGCCAAAT	720
	ACCAGCGGTT GCCACTAA			738
٠, ٠		,	•	
	(2) INFORMATION FOR SEQ ID NO:69:			
45		-	•	
	(i) SEQUENCE CHARACTERISTICS:			•
	(A) LENGTH: 1104 base pairs			
	(B) TYPE: nucleic acid			
	(C) STRANDEDNESS: double			
50	(D) TOPOLOGY: circular			
•	(ii) MOLECULE TYPE: DNA (genomic)	• .		
	(iii) HYPOTHETICAL: NO			
	, <b> / </b>			

```
(iv) ANTI-SENSE: NO
          (vi) ORIGINAL SOURCE:
                (A) ORGANISM: Helicobacter pylori
  5
          (ix) FEATURE:
                (A) NAME/KEY: misc feature
                (B) LOCATION 1...1104
 10
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:
      ATGATTAAAA GCGTAGAGAT TGAAAATTAC AAAAATTTTG AGCACCTTAA AATGGAAAAT
     TTTAAACTCA TCAACTTTTT TACCGGTCAA AACGATGCGG GTAAAACCAA TCTTTTAGAA
                                                                          120
     GCTCTTTATA CCAACACAGG CCTTTGTGAT CCTACTGCCA ATCAAGTCAG TCTTCCTCCT
                                                                           180
     GAACATGCCG TGAATATTAG TGAATTCAGA AAAATCAAAC TCGATGCCGA CAACCTAAAA
15
                                                                          240
      ACCITITITI ATCAAGGAAA CACCGCTAAT CCCATTAGTA TCCGCACTGA ATTTGAACAT
                                                                          300
      GCTACTATCC CTCTTACTAT CCAATACCCC ACACAAACCA GTTACAGCAA AGACATCAAT
                                                                          360
      TTGAATAGCG ATGATGCTCA TATGACAAAC CTTATAAACA CAACAATAAC GAAGCCACAG
                                                                          420
      CTCCAATTTT CCTACAATCC ATCCCTTTCC CCCATGACAA TGACTTATGA ATTTGAAAGG
                                                                          480
20
     CAAAACCTAG GTTTAATCCA TTCTAATTTA GATAAAATCG CTCAAACCTA TAAAGAAAAT
                                                                          540
     GCGATGTTTA TTCCTATAGA ATTATCTATT GTTAATTCTC TTAAAGCATT GGAAAATTTA
                                                                          600
     CAATTAGCAA GCAAAGAAAA AGAATTGATT GAAATCCTAC AATGTTTCAA CCCTAATATT
     TTAAATGCTA ATACAATAAG AAAGTCTGTC TATATCCAAA TCAAAGATGA AAACACACCG
     CTAGAAGAAA GTCCCAAAAG GCTTTTAAAT TTGTTTGGTT GGGGTTTTAT CAAATTCTTT
                                                                          780
     ATTATGGTGA GCATTCTTAT AGACAATCGT GTCAAGTATC TTTTTATTGA TGAAATAGAA
                                                                          840
     AGCGGTTTGC ACCATACAAA AATGCAAGAG TTTTTAAAAG CTCTGTTTAA GTTAGCTCAA
     AAATTACAGA TTCAAATTTT TGCCACCACG CACAATAAGG AATTTTTATT AAACGCCATC
     AACACGATAT CCGATAATGA AACGGGAGTT TTTAAAGACA TAGCCTTGTT TGAGCTTGAA 1020
     AAAGAAAGCG CTTCTGGCTT TATCAGACAC AGCTATTCTA TGCTAGAAAA AGCGCTTTAT
                                                                         1080
     AGGGGTATGG AGGTTAGAGG CTGA
                                                                         1104
     (2) INFORMATION FOR SEQ ID NO:70:
          (i) SEQUENCE CHARACTERISTICS:
35
                (A) LENGTH: 1230 base pairs
                (B) TYPE: nucleic acid
                (C) STRANDEDNESS: double
                (D) TOPOLOGY: circular
40
         (ii) MOLECULE TYPE: DNA (genomic)
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
45
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
50
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...1230
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:
```

660

	·	
	GATCCTTTTG AAACTAAAGA AACGCTAGAA ACGCTAGAAA CGCTTATCAA ACAAACGAGC	120
•	GTTGTTTTAT TGGCCGCTGG GGAGTCTAAG CGTTTTTCTC GTGCGATTAA AAAGCAGTGG	180
	CTACGCTCTC ACCACACCCC CTTATGGCTC AGCGTGTATG AAAGCTTTAA AGAAGCCCTA	240
	GACTTTAAGG AAGTCATTCT AGTTGTAAGC GAATTGGATT ATGTTTATAT CCAACGCCAT	300
5	TACCCCAAAA TCAAGCTTGT AAAAGGCGGG GCATCAAGGC AAGAATCCGT GCGTAACGCT	360
•	TTGAAAGTAA TTGATAGCAC TTACACGATC ACCAGCGATG TGGCTAGGGG TTTAGCGAAT	420
	ATGGAAGCGC TTAAAAGCTT GTTTTTAACC CTCCAACAAA CGAGCCATTA TTGCATCGCC	480
	CCTTACTTGC CTTGCTATGA CACAGCGATC TATTATAACG AGGCTTTAGA TAGAGAAGCG	540
	ATCAAACTCA TTCAAACCCC GCAATTAAGC CACACCAAAA CGCTCCAATC AGCCCTAAAC	600
10	CAAGGGGGTT TTAAAGATGA AAGCAGCGCG ATTTTACAAG CTTTCCCTAA CTCTGTGAGC	660
	TATATTGAAG GCAGTAAGGA TTTGCACAAA CTCACCACAA GCGGCGATTT AAAGTTTTTT	720
	ACGCCTTTTT TTAACCCAGC AAAGGACACT TTTATAGGCA TGGGTTTTGA TACGCATGCG	780
	TTCATTAAAG ATAAGCCTAT GGTTTTAGGG GGGGTTGTTT TGGATTGCGA GTTTGGGTTA	840
	AAGGCTCATA GCGATGGCGA TGCTTTATTG CATGCGGTTA TTGATGCGAT TTTAGGAGCG	900
15	ATTAAAGGG GGGATATTGG CGAATGGTTC CCTGATAATG ACCCCAAATA CAAAAACGCC	960
	TCTTCTAAAG AGCTTTTAAA AATCGTGTTG GATTTTTCTC AAAGCATTGG GTTTGAATTG	1020
	CTTGAAATGG GAGCGACCAT CTTTAGCGAA ATCCCTAAAA TCACTCCTTA CAAACCGGCG	1080
	ATTTTAGAGA ATTTGAGCCA ACTTTTGGGT TTAGAAAAAT CTCAAATCAG CTTGAAAGCC	1140
	ACTACAATGG AAAAAATGGG GTTCATTGGC AAACAAGAAG GGCTGTTAGT CCAAGCGCAT	1200
20	GTGAGCATGC GTTATAAACA AAAACTTTAA	1230
	(2) INFORMATION FOR SEQ ID NO:71:	
	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 813 base pairs	
	(B) TYPE: nucleic acid	
	(C) STRANDEDNESS: double	
	(D) TOPOLOGY: circular	
30		
30	(ii) MOLECULE TYPE: DNA (genomic)	
	4444	
	(iii) HYPOTHETICAL: NO	
25	(iv) ANTI-SENSE: NO	
35		
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Helicobacter pylori	
	// \	
40	(ix) FEATURE:	
40	(A) NAME/KEY: misc_feature	•
	(B) LOCATION 1813	
	(a) CROWNIGH BRIGHT BRIGHT BRIGHT BRIGHT	
•	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:	
15	3.003.3.3.3.2.CM (MMCM) COMMIN	
45	ATGAAAAAGT TTGTAGCTTT AGGGCTTCTA TCCGCGGTTT TAAGCTCTTC GTTGTTAGCC	60
	GAAGGTGATG GTGTTTATAT AGGGACTAAT TATCAGCTTG GACAAGCCCG TTTGAATAGC	120
	AATATTTATA ATACAGGGGA TTGCACAGGG AGTGTTGTAG GTTGCCCCCC AGGTCTTACC	180
	GCTAATAAGC ATAATCCAGG AGGCACCAAT ATCAATTGGC ACTCCAAATA CGCTAATGGG	240
50	GCTTTGAATG GTTTTGGGTT GAATGTGGGT TATAAGAAAT TCTTCCAATT CAAGTCGCTA	300
50	GATATGACAA GCAAGTGGTT TGGTTTTAGA GTGTATGGGC TTTTTGATTA CGGGCATGCC	360
	GATTTAGGTA AACAAGTTTA TGCACCTAAT AAAATCCAGT TGGATATGGT CTCTTGGGGT	420
	GTGGGGAGCG ATTTGTTAGC TGATATTATT GATAAAGACA ACGCTTCTTT TGGTATTTTT	480
	GGTGGGGTCG CTATCGGCGG TAACACTTGG AAAAGCTCTG CAGCAAACTA TTGGAAAGAG	540
e e	CAAATCATTG AAGCCAAAGG TCCTGATGTT TGTACCCCTA CTTATTGTAA CCCTAATGCC	600
55	CCTTATACCA CCAACACTTC AACCCTCCCT TTTCAACTCT CCCTCAAAAAAAA	CC0

CCTTATAGCA CCAACACTTC AACCGTCGCT TTTCAAGTGT GGTTGAATTT TGGGGTGAGA

GCCAATATCT ACAAGCATAA TGGCGTGGAA TTTGGCGTGA	GAGTGCCGCT	ACTCATCAAT	720
AAATTTTTGA GCGCGGGTCC TAACGCTACT AACCTTTATT	' ACCATTTGAA	ACGGGATTAT	780
TCGCTTTATT TGGGGTATAA CTACACTTTT TAA		*	813
		•	
(2) INFORMATION FOR SEQ ID NO:72:	•		
			-
(i) SEQUENCE CHARACTERISTICS:			٠
(A) LENGTH: 1317 base pairs			
(B) TYPE: nucleic acid	•		
(C) STRANDEDNESS: double	•		
(D) TOPOLOGY: circular			
(ii) MOLECULE TYPE: DNA (genomic)			
(****)			
(iii) HYPOTHETICAL: NO			
(iv) ANTI-SENSE: NO			
4-30			
(vi) ORIGINAL SOURCE:			
(A) ORGANISM: Helicobacter pylori			
(1)			
(ix) FEATURE:			
(A) NAME/KEY: misc_feature		•	
(B) LOCATION 11317			
(with Grouping programmers			
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72	•		
ATCCCTTACA AACCTAACAA AAACAACTTA AAACAACTTA			
ATGGCTTACA AACCTAACAA AAAGAAGTTA AAAGAATTAA	GAGAGCAACC	GAATTTATTT	60
AGCATCTTAG ATAAGGGCGA TGTTGCAACA AACAATCCTG	TTGAAGAGTC	AGACAAGGCC	120
AATAAAATAC AAGAGCCACT CCCTTATGTC GTGAAAACGC	AAATCAATAA	AGCAAGCATG	180
ATTTCTAGAG ATCCTATTGA ATGGGCAAAG TATTTAAGCT	TTGAAAAACG	AGTCTATAAG	240
GATAATAGTA AAGAAGATGT CAATTTCTTT GCCAATGGTG GTTTATGAAG CGAATAAAGA AGGGTTTGAA AGGCGCATCA	AGATAAAAGA	AAGTTCTCGT	300
GATAGAAATA TTGATAGAAA TAGAGAATTT TTTATAAAAG	CTAAAAGATA	CGATCTGATT	360
ACADACACCE TANDACAMER CARACACAR COCERTAIN	AAATTGAAAT	TCTAACCCAC	420
ACAAACAGCT TAAAAGAATT GAAAGAGCAA GGGTTAGAAA GAAACGCATA AGAAAGCCTT AGAAAATGGC AATGAAATCG	TCCAATTGAC	CCACCATAAT	480
AAAGATATTT ACCAAGAAGT AGAAAGAACA AAAGATGGTG	TTAAAGAATA	CGACCATCTT	540
CCCAGTATTT CTAGCGCTGA GTATTTCAAG CTTTACAACA	GATTGGTAAG	AGAAATAATC	600
AACAATGAAA ATACCAAACT GAATACTAAC GACAATGAAG	AACTGCCTTT	TGAATCAATA	660
GAATTAGCTA AAGAAGTGCA TATTTTAATC CTAGAGCAAC	AAGTTAAAAA	ACTAGAATTT	720
TATTATTCTT GGATAGATAA AGATGATAAT GCGAATTTTG	AATTGCTTTC	AGCAACAAAT	780
ATCAATGAAA ATAAACTCAA AGAAAACCAT CTCAGCGCCA	CTTGGAAAAT	GCATAGGCTT	840
CAATTTTCT TTAATAATGG TTCTATTTTA GGCTGGACTA	ATAACGCTAA	TAAGATTAAG	900
CAAGAAAACA GAGATTATTC TTTAAGAAGC GCTCTTTTAA	AAGAAGAACA	AAGCGCTATA	960
GCAAAATTG AATTGCAAAA ATAGTATGAA AGGGTTTAA	GTTTAGAAGA	AATCGCTCAA	1020
GCAAAAATTG AATTGCAAAA ATACTATGAA AGCGTTTATG	TTAATGGTGA	TGGGAATAAA	1080
AGAGAAATCA AGCCTTTTAA AGAAATTTTA AGAGACACCA	ACAATITTGA	AAAAGCTTAT	1140
AAGGAGCGTT ATGACAAATT GGTAAGCTTG AGTGCAGCAA	TCATTCAAGC	TAAAGAGGGT	1200
GGTAATGAGC GACCAAATTC TAGTGCAAAT AACAATAACC	CTATTAAAAA	TACAATAGAG	1260
ACTAATACTT CTAACAATAT TATTCAAAAT AATGATAATA	TAATCATCCA	AATTTAA	1317
(2) INFORMATION FOR SEQ ID NO:73:			
(a) and olders tour dry ID MO:/3:	•		

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 648 base pairs
(B) TYPE: nucleic acid

- 143 -

	(C) STRANDEDNESS: double (D) TOPOLOGY: circular
5	(ii) MOLECULE TYPE: DNA (genomic)
	(iii) HYPOTHETICAL: NO
	(iv) ANTI-SENSE: NO
10	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1648</pre>
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:
20	ATGCAAGCGT TAAAATCATT GCTTGAAGTG ATTACAAAAC TCCAGAATCT AGGCGGCTAT 60 TTGATGCATA TAGCTATTTT CATCATTTTT ATTTGGATTG GAGGGCTTAA GTTTGTGCCT 120 TACGAAGCTG AAGGGATCGC CCCTTTTGTG GCCAACTCCC CTTTCTTTTC TTTCATGTAT 180 AAATTTGAAA AACCTGCATA CAAACAACAC AAAATGTCTG AATCCCAATC CATGCAAGAA 240
25	GAAATGCAAG ATAACCCTAA AATCGTTGAA AACAAAGAAT GGCATAAAGA AAACCGCACT 300 TATTTAGTGG CTGAAGGTTT AGGGATTACG ATCATGATCC TAGGCATTTT GGTGCTTTTG 360 GGGCTTTGGA TGCCTTTAAT GGGCGTAGTT GGGGGCTTGC TTGTCGCTGG AATGACGATC 420 ACCACCCTAT CTTTTTATT CACAAACGCCA GAAGTGTTTG TCAATCAGCA TTTCCCATGG 480 CTTTCTGGGG CTGGAAGGCT AGTGGTTAAA GACTTGCGT TATTTGCTGG AGGCTTGTTT 540
30	GTGGCCGGAT TTGATGCGAA ACGCTATTTG GAGGGTAAAG GGTTTTGCTT GATGGACCGC 600 TCATCGGTAG GGATTAAAAC TAAATGCTCT AGCGGGTGTT GCTCTTAA 648  (2) INFORMATION FOR SEQ ID NO:74:
35	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 186 amino acids</li><li>(B) TYPE: amino acid</li><li>(D) TOPOLOGY: linear</li></ul>
	(ii) MOLECULE TYPE: protein
40	(iii) HYPOTHETICAL: YES
	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori
45	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 1186</pre>
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:
50	Met Ile Lys Arg Ile Ala Cys Ile Leu Ser Leu Ser Ala Ser Leu Ala
	1 5 10 15 Leu Ala Gly Glu Val Asn Gly Phe Phe Met Gly Ala Gly Tyr Gln Gln
55	20 25 30 Gly Arg Tyr Gly Pro Tyr Asn Ser Asn Tyr Ser Asp Trp Arg His Gly

			35				°₹	40					45			
	Asn	Asp 50	Leu	Tyr	Gly	Leu	Asn 55		Lys	Leu	Gly	Phe		Gly	Phe	Ala
5	65					70					75	Leu		Trp		80
					85					90				Tyr	95	Gl
••				100					105					Phe 110	1	1.71
10			115					120					125	Met		
		130					135					140		Leu		
15	145					150					155			Val		160
					165					170		Leu	Ile	Arg	Tyr 175	Tyr
20	"Şer	тър	Tyr	180	Asp	Tyr	Val	Phe	Thr 185	Phe				-		
20	(2)	INFO	RMA!	rion	FOR	SEQ	ID	NO : 7	5 :							
25		(i)	. (J	A) LI 3) T		H: 1: ami	16 ai	ISTIC mino cid		ds	·	٠				
1		(ii)			:			tein					٠			
30	(	: <i>,</i>				•		CCIII								
		(vi)			AL SC			icoba	actei	r py]	lori		:			٠
35		(ix)	(A	TURE L) NZ L) LC		CEY:	misc	c_fea L16	ture	<b>.</b>						
10	٠	(xi)	SEÇ	UENC	E DE	SCR	PTIC	ON: S	SEQ 1	D NO	):75	: .	-	•		
	Leu 1	Met .	Arg	Ile	Ile 5	Ile	Arg	Leu	Leu	Ser 10	Phe	Lys	Met	Asn	Ala 15	Phe
				20					25					Tyr 30	Ala	
<b>\$</b> 5			35					40					45	Val		
		50					55					60				
50	Arg (					70			* 1		75					80
	Ile				85					90					95	Ala
· E	Lys 1			100	Glu	Ser	Arg	Gln	Lys 105	Gln	Asp	Leu	Lys	Glu 110	Gln	Met
55	Lys 1	ьув :	ryr .	Ser								*				

WO 98/18323

115

#### (2) INFORMATION FOR SEQ ID NO:76:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 345 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

15 (A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

(A) NAME/KEY: misc feature

(B) LOCATION 1...345

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

Met Val Lys His Tyr Leu Phe Met Ala Val Ser Gln Val Phe Phe Ser 25 Phe Phe Leu Val Leu Phe Phe Ile Ser Ser Ile Val Leu Leu Ile Ser Ile Ala Ser Val Thr Leu Val Ile Lys Val Ser Phe Leu Asp Leu Val 40 Gln Leu Phe Leu Tyr Ser Leu Pro Gly Thr Ile Phe Phe Ile Leu Pro 30 55 Ile Thr Phe Phe Ala Ala Cys Ala Leu Gly Leu Ser Arg Leu Ser Tyr 70 75 Asp His Glu Leu Leu Val Phe Phe Ser Leu Gly Val Ser Pro Lys Lys 85 90 35 Met Thr Lys Ala Phe Val Pro Leu Ser Leu Val Ser Ala Ile Leu 105 Leu Ala Phe Ser Leu Ile Leu Ile Pro Thr Ser Lys Ser Ala Tyr Tyr 120 Gly Phe Leu Arg Gln Lys Lys Asp Lys Ile Asp Ile Asn Ile Arg Ala 135 Gly Glu Phe Gly Gln Lys Leu Gly Asp Trp Leu Val Tyr Val Asp Lys 150 Thr Glu Asn Asn Ser Tyr Asp Asn Leu Val Leu Phe Ser Asn Lys Ser Leu Ser Gln Glu Ser Phe Ile Leu Ala Gln Lys Gly Asn Ile Asn Asn Gln Asn Gly Val Phe Glu Leu Asn Leu Tyr Asn Gly His Ala Tyr Phe 200 Thr Gln Gly Asp Lys Met Arg Lys Val Asp Phe Glu Glu Leu His Leu 50 215 Arg Asn Lys Leu Lys Ser Phe Asn Ser Asn Asp Ala Ala Tyr Leu Gln 235 Gly Thr Asp Tyr Leu Gly Tyr Trp Lys Lys Ala Phe Gly Lys Asn Ala 250

Asn Lys Asn Gln Lys Arg Arg Phe Ser Gln Ala Ile Leu Val Ser Leu

				0.50												
	Dhe	Pro	T.011	260	Sor	Va 1	Dhe	Len	265	Dwo	T 011	Dho	C1.,	270	71-	2
			275					280					285			
5		Arg 290					295					300				
	305	Val	,			310					315					320
	Met	Thr	Phe	Phe	Phe 325	Pro	Phe	Ile	Trp	Ala 330	Phe	Ile	Ser	Tyr	Leu 335	Leu
10	Phe	Arg	Lys	Phe 340	Ile	Leu	Lys	Arg	Tyr 345							
	(2)	INF	ORMA!	rion	FOR	SEQ	ו מו	NO: 7	7 : ;							
15		(i)	(1	A) LI B) T	ENGTI YPE :	HARAC H: 2' amin OGY:	76 ar	mino cid		is						
20		(ii)	MO	LECUI	LE T	YPE:	pro	tein								
		(iii)	HY	POTHI	ETIC	AL: Y	YES									
25		(vi)				OURCI ISM:		icoba	acte	r py:	lori					
		(ix)	()		ame/1	KEY:			ature	<b>≥</b>						
30			(1	B) L(	CAT.	ION :	1:	276								
		(xi)	SE	QUENC	CE DI	ESCR:	[PTI	ON: S	SEQ .	ID NO	):77	:				
	Met 1	Lys	Lys	Lys	Ala 5	Lys	Val	Phe	Trp	Cys 10	Cys	Phe	Lys	Met	Ile 15	Arg
35	Trp	Leu	Tyr	Leu 20	Ala	Val	Phe	Phe	Leu 25	Leu	Ser	Val	Ser	Asp 30	Ala	Lys
	Glu	Ile	Ala 35	Met	Gln	Arg	Phe	Asp 40	Lys	Gln	Asn	His	Lys 45	Ile	Phe	Glu
40	Ile	Leu 50	Ala	Asp	Lys	Val	Ser 55	Ala	Lys	Asp	Asn	Val 60	Ile	Thr	Ala	Ser
	65	Asn				70					75					80
	Val	Arg	Tyr	Asp	Thr 85	Lys	Thr	Lys	Glu	Ala 90	Leu	Leu	Glu	Gly	Asn 95	Ile
<b>4</b> 5	Lys	Val	Tyr	Arg 100	Gly	Glu	Gly	Leu	Leu 105	Val	Lys	Thr	Asp	Tyr 110	Val	Lys
	Leu	Ser	Leu 115	Asn	Glu	Lys	Tyr	Glu 120	Ile	Ile	Phe	Pro	Phe 125	Tyr	Val	Gln
50		Ser 130					135					140				
		Gln	Lys	Tyr	Lys		Lys	Asn	Met	Ser	Ala	Ser	Gly	Cys	Ser	Ile
	145	N ~~	D~~	т1 ~	П	150	1707	n	<b>77</b> -	m.	155	<b>~</b> ?	0 -	D1	<b>3</b>	160
	wsb	Asn	FIO	TTG	165	uts	val	ASII	ATS	170	ser	GTÅ	ser	rne	175	Met
55	${\tt Gln}$	Lys	Ser	His	Leu	Ser	Met	Trp	Asn		Lys	Ile	Tyr	Val		Asp

				180					185					190		
	Ile	Pro	Val 195	Leu	Tyr	Leu	Pro	Tyr 200	Ile	Phe	Met	Ser	Thr 205	Ser	Asn	Lys
5	Arg	Thr 210	Thr	Gly	Phe	Leu	Tyr 215	Pro	Glu	Phe	Gly	Thr 220	Ser	Asn	Leu	Asp
	225			Tyr		230			-		235	•				240
• •	_			Phe	245				_	250			_		255	
10				Ala 260	Arg	Tyr	Ile	Asn	Ser 265	Lys	Thr	Gln	Val	Phe 270	Ile	Gln
	Cys	Ala	Leu 275	Pne								. •				
15	(2)	INFO	ORMA!	rion	FOR	SEQ	ID 1	NO: 78	3:							
***		(i)	-	A) ri Saeno						is						
20				3) T? (C) T(												
		(ii)	MOI	LECUI	LE T	YPE:	prot	cein								
25	- 1	(iii)	НҮІ	POTHI	ETIC	AL: Y	ÆS		•							
		(vi)		IGINA A) OI				icoba	acte	r pvi	lori					
		(ix)		ATURI						- 1-1						
30				A) NA B) L				_	ature	9						
		(xi)	SEÇ	QUENC	CE DI	ESCR	[PTIC	ON: S	SEQ :	ID N	D:78					
35	Met 1	Ile	Arg	Leu	Lys 5	Gly	Leu	Asn	Lys	Thr	Leu	Lys	Thr	Ser	Leu 15	Leu
	_	Gly	Val	Leu 20	Leu	Gly	Ala	Thr	Ala 25		Leu	Met	Ala	Lys 30		Leu
40	Leu	Ser	Asp 35	Glu	Asp	Leu	Leu	Lys 40	Arg	Val	Lys	Leu	His 45	Asn	Ile	Lys
	Glu	Asp 50	Thr	Leu	Thr	Ser	Cys 55	Asn	Ala	Lys	Val	Asp 60	Gly	Ser	Gln	Tyr
4.5	65			Gly		70					75					80
45				Phe	85				•	90					95	
				Asn 100			-		105	_	_			110		
50			115	Glu				120		_			125		-	
		130		Glu			135					140				
55	145			Thr		150			·		155		-		•	160
					5			3		1	1	~		3		

					165					170		٠.			175	•
				180				Lys	185					190		
5 .			195					Ile 200					205			
	Lys	Lys 210	Ala	Leu	Met	Ile	Leu 215	Asp	Asn	Pro	Tyr	Leu 220	Leu	Trp	Leu	Val
10	(2)	INF	ORMA'	rion	FOR	SEQ	ID 1	NO:7	9:							
		· (i	(2 (1		engti YPE :	H: 42	29 at			ds						
15		(ii)	•	LECU	•					•						
		(iii	HY	POTH	ETIC	AL: 1	YES									
20		(vi		IGINZ A) OI				icoba	acte	r py:	lori					
		(ix		ATURI		KEV.	mie	c_fea	a + 11 × 4	_						
25				B) L(					acur	<b>-</b>						
		(xi	) SE(	QUEN	CE D	ESCR:	IPTI(	ON: S	SEQ :	ID NO	0:79	:				
30	Met 1	Pro	Tyr	Ala	Leu 5	Arg	Lys	Arg	Phe	Phe 10	Lys	Arg	Leu	Leu	Leu 15	Phe
				20				Asn	25					30	•	
25			35					Gln 40					45			
35	Ser	50					55					60				.*
	65					70		Asn Lys			75	٠.			*	80
40					85			Tyr		90					95	
-				100				Gly	105					110		
45	•		115					120 Thr					125			
		130					<b>135</b>	Ser				140				
	145		-			150					155					160
50					165			Phe		170					175	,
				180					185			•		190		
55			195					Lys 200			Leu	Glu	Asn 205		Thr	Glu

•		210					215					220				
	Gln	T.61)	Glv	Met	Leu	Ala	Thr	Phe	Ile	Ser	Pro	Asn	Ser	Pro	Val	Ile
	225		<b>-</b>			230					235					240
		The exact	N ars	Acn	λen	Gly	T.e.11	Tle	Glv	Glu		Len	Ara	Gln	Tle	Thr
5	GIU	TAT	Map	АБР	245	Gry	DCu	110	Gry	250		<b></b>	**-5	V	255	
5		_	_	•		~1	77 T	T	77.2 -		<b>01.</b>	<b>&gt;</b>	T1.	C-~		Tare
	GIu	Ser	Leu		vaı	Glu	vaı	гля		GIII	GIU	ASII	TTE			шуs
				260					265			·	_	270		_,
	Gln	Ala	Thr	Ser	Phe	Ser	Lys	Asn	Phe	Arg	Lys	His	Asp	Ala	Pne	Phe
			275					280					285			- <
10	Lys	Asn	Ser	Thr	Leu	Ile	Leu	Asn	Thr	Pro	Thr	Thr	ГÀЗ	Ser	Gly	Leu
		290					295.					300				
	Ile	Leu	Ser	Gln	Ile	Gly	Leu	Leu	Glu	Tyr	Lys	Pro	Leu	Lys	Ile	Leu
	305					310					315					320
		Thr	Gln	Ile	Asn	Phe	Asn	Pro	Ser	Leu	Leu	Leu	Leu	Thr	Gln	Pro
15				7.	325					330					335	
1.5	Larg	Nen	Δνα	Lve		Leu	Phe	Tle	Val		Ala	Leu	Gln	Asn	Ser	Asp
	Буз	ASP	nr 9	340					345					350		
	<b>~</b> 1	mb	T 011		Cli	Tyr	712	Sor		T.011	Glu	Car	Δen		Δτα	His
	GIU	THE		116	GIU	TYL	ALG		пец	Бец	GLU	261	365			
20	_	<b></b>	355	<b>.</b>				360	T1_	a1	T	<b>63.</b> 1		Dha	Lan	Nen
20	Asp	_	vai	ASII	Tyr	Ser		ALG	116		ьеи		Met	FILE	пси	No.
		370	_	_			375	•			~1 -	380	<b></b>	T	<b>~</b> 1	N an
		Leu	Asp	Pro	HIS	Phe	гÃг	гÀз	ser	Pne		GIU	261	геп	GIU	
	385					390				_	395		_			400
	Asn	Gln	Val	Arg		His	Asn	Gln	Ile		GIn	Ala	Leu	GIA		ser
25					405					410					415	
	Phe	Glu	Pro	Ile	Lys	Asn	Glu	Ser	Glu	Thr	Lys	Lys	Glu			
				420					425							
								,								
	(2)	INF	'AMRC	TION	FOR	SEQ	ID !	8:07	0:							
30																
		(i	) SE	QUEN	CE C	HARA	CTER	ISTI	CS:							
			()	A) Li	ENGT	H: 4	55 aı	mino	aci	ds						
			(	B) T	YPE:	ami	no a	cid								
	9.		(	D) T	OPOL	OGY:	lin	ear								
35														,		
		(ii	) MO	LECU	LE T	YPE:	pro	tein								
					•											
		(iii	) HY	POTH	ETIC	AL:	YES									
					•											
40		(vi	) OR	IGIN	AL S	OURC	E:									
		•				ISM:		icob	acte	r py	lori					
			•	,			,				•					
		lix	) FE	ATUR	E :							9.4				
		(	•			KEY:	mis	c fe	atur	e						
45						ION.		_					•			
43		·	`	J, <u>J</u>	· · · · ·											
•		1-4	) CP	OTTEN	מב ה	ESCR	דייים	ON .	SEO	א מד	n - 80					
		(XI	, 35	COEM	כם ט	Bock		011.		II	٠٠٠٠	•				
	77-7	T	7	nh.		Tare	T.ess	D~~	Len	T.en	Dho	17=1	Ser	Tle	Ţ,aıı	Tyr
50		Leu	гув	Pne	GTII	nys	Deu	PIO	Deu	_	FILE	var	Jer	110	15	-7-
50	1		_	_	5	•		Dh.a	3	10	7	Dho	0	<i>α</i> 1		ת 7 ת
	Asn	Gin	Ser		Leu	Leu	Ата	Pne		Tyr	гÀг	Pne	Ser		Val	MIG
•	. =			20	_		~3		25			<b>T</b>	T	30		T
	Glu	Ser		Ser	rys	Val	GLY		Asn	His	ser	ьys		Asn	ser	ьys
			35					40					45			
												_ ~			-	•
55	Glu	Gly	Ile	Phe	Pro	Thr	Ala	Thr	Phe	Val	Thr	Ala	Thr	Ile	Lys	Leu

		50					55					60				
	Gln	Val	Asp	Ser	Asn	Leu	Leu	Pro	Lys	Asn	Ile	Glu	Lys	His	Ser	Leu
	65					70					75					80
	Lys	Ile	Gly	Val	Gly	Gly	Ile	Leu	Gly	Ala	Leu	Ala	Tyr	Asp	Ser	Thr
5	•		•		85	-			•	90	•		<b>-</b> .	-	95	
	Lvs	Thr	Leu	Ile	Asp	Gln	Ala	Thr	His	Gln	Ile	Tvr	Glv	Ser	Glu	Leu
	-1-			100					105			2 -	1	110		
	Dho	Trans	T.011		Glv	λνα	Trees	Trr.		Dho	Leu	Gl <sub>3</sub> z	λen	Ala	Dro	Trn
	FIIC	-y-	115	110	- Y	AL 9	11p	120	Gry	FIIG	Deu	GLY	125	ALG.	110	ııp
10	<b>.</b>			T	T1.		C		<b>7.7</b> -	*** -	m			Ma saa	777	*
10	гуѕ	_	Ser	Deu	116	GIU		MSP	ALA	urs	1111			Tyr	var	neu
	_	130	<b>a</b> :	<b>~</b>	T	nh -	135	0	<b></b>	<b>~</b> 1	•	140		***	<b>T</b>	T
	-	Asn	ser	Tyr	Leu		TYL	ser	Tyr	_	-	ьys	Pue	His	Leu	
	145			_	_	150	_		_		155	_	_	_		160
1.5	Leu	GLY	Arg	ıyr		ser	Asn	Met	Asp		Met	ser	ser	Tyr		GIN
15				_	165	_	_			170				_	175	_
	Gly	Phe	Glu		Asp	Tyr	Lys	Ile		Ser	Lys	Ile	Ala	Leu	Lys	Trp
•				180					185					190	•	
*	Phe	Ser	Ser	Phe	Gly	Arg	Ala	Leu	Ala	Phe	Gly	Gln	Trp	Ile	Arg	Asp
			195					200					205			
20	Trp	Tyr	Ala	Pro	Ile	Val	Thr	Glu	Asp	Gly	Arg	Lys	Glu	Val	Tyr	Asp
		210					215					220				
	Gly	Ile	His	Ala	Ala	Gln	Leu	Tyr	Phe	Ser	Ser	Lys	His	Val	Gln	Val
	225					230					235					240
	Met	Pro	Phe	Ala	Tyr	Phe	Ser	Pro	Lys	Ile	Tyr	Gly	Ala	Pro	Gly	Val
25					245					250					255	
	Lys	Ile	His	Ile	Asp	Ser	Asn	Pro	Lys	Phe	Lys	Gly	Leu	Gly	Leu	Arg
				260					265	*				270	•	
	Ala	Gln	Thr	Thr	Ile	Asn	Val	Ile	Phe	Pro	Val	Tyr	Ala	Lys	Asp	Leu
			275					280				_	285			
30	Tyr	Asp	Val	Tyr	Trp	Arg	Asn	Ser	Lys	Ile	Gly	Glu	Trp	Gly	Ala	Ser
•	_	290		_			295		_		_	300				
	Leu	Leu	Ile	His	Gln	Arg	Phe	Asp	Tyr	Asn	Glu	Phe	Asn	Phe	Gly	Phe
	305					310		_			315				=	320
	Gly	Tyr	Tyr	Gln	Asn	Phe	Gly	Asn	Ala	Asn	Ala	Arq	Ile	Gly	Trp	Tyr
35	•	•	-		325		•			330		_		-	335	-
	Glv	Asn	Pro	Ile	Pro	Phe	Asn	Tvr	Arg		Asn	Ser	Val	Tyr		Glv
	•			340				. 1	345			•	-	350	•	-
	Val	Phe	Ser	Asn	Ala	Ile	Thr	Ala		Ala	Val	Ser	Glv	Tyr	Val	Phe
			355					360					365	-1-		
40	Glv	Glv		Val	Tvr	Ara	Glv		Leu	Tro	Glv	Ile		Gly	Ara	Tvr
• •	1	370			-1-						1	380		1	3	-3-
	Thr			Thr	Δτα	Δla					Tla			λαή	T.011	Gly
	385	-1-			• 9	390		014	***9	501	395	*****	<b></b>	21011		400
		Lare	מרגע	Gl <sub>3</sub> z	Sar		Λl =	D.r.c.	V-1	Acn		λen	T.ou	Glu	There	
45	T Y T	Lys	115	Gry	405	FIIC	ALG	мy	Val	410	Val	Vali	пеа	GIU	415	TYL
73	1701	1701	C 0 **	Mot		λα»	Ċl.	The east	7		3	The same	T 011	mb~		Dwo
	val	val	Ser			ASII	Grå	ıyı	_	neu	Asp	ıyı	Leu	Thr	GIŞ	PIO
	D	N'	7	420		T	n 7 -	7	425	<b>~1</b>	<b>3</b>	<b>3</b>		430	T	Me -
	rue	ASI		WTG	Lue	гÀЗ	WTG		ATG	GIN	Asp	arg		Asn	Leu	Mec
50			435	<b>.</b>	73.	D1 :	D)	440					445			
50	val		Met	гуз	Phe	hue										
		450				•	455									*
													,			

- (2) INFORMATION FOR SEQ ID NO:81:
- 55 (i) SEQUENCE CHARACTERISTICS:

WO 98/18323 PCT/US97/19575

- 151 -

(A) LENGTH: 282 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

10 (A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

(A) NAME/KEY: misc\_feature

(B) LOCATION 1...282

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

Met Gly Cys Ser Phe Ile Phe Lys Lys Val Arg Val Tyr Ser Lys Met

1 5 10 15

20 Leu Val Ala Leu Gly Leu Ser Ser Val Leu Ile Gly Cys Ala Met Asn 20 25 30

Pro Ser Ala Glu Thr Lys Lys Pro Asn Asp Ala Lys Asn Gln Gln Pro 35 40 45

Val Gln Thr His Glu Arg Met Thr Thr Ser Ser Glu His Val Thr Pro 55 60

Leu Asp Phe Asn Tyr Pro Val His Ile Val Gln Ala Pro Gln Asn His 65 70 75 80

His Val Val Gly Ile Leu Met Pro Arg Ile Gln Val Ser Asp Asn Leu 85 90 95

O Lys Pro Tyr Ile Asp Lys Phe Gln Asp Ala Leu Ile Asn Gln Ile Gln 100 105 110

Thr Ile Phe Glu Lys Arg Gly Tyr Gln Val Leu Arg Phe Gln Asp Glu 115 120 125

Lys Ala Leu Asn Val Gln Asp Lys Lys Ile Phe Ser Val Leu Asp
35 130 135 140

Leu Lys Gly Trp Val Gly Ile Leu Glu Asp Leu Lys Met Asn Leu Lys 145 150 155 160

Asp Pro Asn Ser Pro Asn Leu Asp Thr Leu Val Asp Gln Ser Ser Gly
165 170 175

40 Ser Val Trp Phe Asn Phe Tyr Glu Pro Glu Ser Asn Arg Val Val His
180 185 190

Asp Phe Ala Val Glu Val Gly Thr Phe Gln Ala Ile Thr Tyr Thr Tyr 195 200 205

Thr Ser Thr Asn Asn Ala Ser Gly Gly Phe Asn Ser Ser Lys Ser Val
45 210 215 220

Ile His Glu Asn Leu Asp Lys Asn Arg Glu Asp Ala Ile His Lys Ile
225 230 235 240

Leu Asn Arg Met Tyr Ala Val Val Met Lys Lys Ala Val Thr Glu Leu 245 250 255

50 Thr Lys Glu Asn Ile Ala Lys Tyr Arg Asp Ala Ile Asp Arg Met Lys 260 265 270

Gly Phe Lys Ser Ser Met Pro Gln Lys Lys 275 280

55 (2) INFORMATION FOR SEQ ID NO:82:

		(1	.) SE												*	
								mino	aci	ds						
5				B) T										•		
3			(	D) T	OPOL	OGY:	lin	ear								
		/ 4 4	) мо	י דיריוז	 T.Er: ∕rr	VDE.										
		, ,	, 140	LECO	<b>11</b> 12 1	IPE:	pro	cein								
	٠	(iii	) HY	РОТН	ETIC	AL:	YES		•							
10		•					777		٠.	5						
		(vi	) OR	IGIN	AL S	OURC	E:		•							
•			. (	A) O	RGAN	ISM:	Hel	icob	acte	r py	lori			•		
15		(ix	) FE					_								
13				A) N B) L				c_fe	atur	e						
			•	Б, Ц	OCAI	TON	1	280							•	
		(xi	) SE	QUEN	CE D	ESCR	IPTI	ON:	SEO	TD N	0+82					
				_							0.02	•				
20	Met	Lys	Leu	Arg	Ala	Ser	Val	Leu	Ile	Gly	Val	Ala	Ile	Leu	Cys	Let
	1				5					10					15	
	Ile	Leu	Ser		Суѕ	Ser	Asn	Tyr		Lys	Lys	Val	Val	Lys	Gln	Lys
	Δen	Hie	Val	20	ጥኮሎ	Dro	1707	The same	25	<b>01</b>	<b>*</b>	-1.	~3	30	_	_
25			35		1111	FIU	Vai	40	ASII	GIU	Leu	ire	45	ràs	Tyr	Sei
	Glu	Ile	Pro	Leu	Asn	Asp	Lys		Lys	Asp	Thr	Pro		Met	Val	Glr
		50				_	55					60				
	Val	Lys	Leu	Pro	Asn	Tyr	Lys	Asp	Tyr	Leu	Leu	Asp	Asn	Lys	Gln	Va]
20	65					70					75					80
30	Val	Leu	Thr	Phe		Leu	Val	His	His		Lys	Lys	Ile	Thr	Leu	Ile
	Glv	Asn	Ala	λen	85 Tare	Tla	Lou	Cln	The same	90	N		D1	<b>~</b> 3	95	
	u.,		mid	100	шув	116	neu	GIII	105	тĀR	ASI	Tyr	Pne	110	Ala	AST
	Gly	Ala	Arg	Ser	Asp	Ile	Asp	Phe		Leu	Gln	Pro	Thr		Asn	Glr
35			115					120					125			
	Lys	Gly	Val	Val	Met	Ile	Ala	Ser	Asn	Tyr	Asn	Asp	Asn	Pro	Asn	Asn
	•	130	_	_			135					140				
	ьуs 145	GIU	Lys	Pro	Gin		Phe	Asp	Val	Leu		Gly	Ser	Gln	Pro	
40	_	Glv	Ala	Δgn	ጥከተ	150	λen	T.ou	uic	c1	155	7	***	<b>a</b>	<b>~</b> 1	160
		1		•••	165	y	71511	Deu	што	170	TAT	Asp	Val	ser	175	Ala
	Asn	Asn	Lys	Gln		Ile	Asn	Glu	Val		Ara	Glu	Lvs	Ala	Gln	Leu
				180					185					190		
45	Glu	Lys	Ile	Asn	Gln	Tyr	Tyr	Lys	Thr	Leu	Leu	Gln	Asp	Lys	Glu	Gln
45	<b>63</b>	m	195			_		200					205			
	GIU	1yr 210	Thr	Thr	Arg	Lys		Asn	Gln	Arg	Glu		Leu	Glu	Thr	Leu
*.	Ser		Arg	Δla	Glv	Tree	215 Gln	Mot	7~~	C1	· .	220	<b>73</b> -	<b>a</b>	0	<b>~</b> 3
	225		9		OL,	230	ÓIII	Mec	Arg	GIII	235	Val	TTE	ser	ser	240
50	Ile	Phe	Lys	Asn	Gly		Leu	Asn	Met	Gln		Lvs	Glu	Glu	Glu	
					245					250					255	
	Arg	Glu	Lys		Gln	Glu	Glu	Arg		Asn	Glu	Tyr	Leu	Arg	Asn	Gln
	•			260					265					270		
55	ile	Arg	Ser 275	Leu	Leu	Ser	Gly									
			213					280								

```
(2) INFORMATION FOR SEQ ID NO:83:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 393 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
        (ii) MOLECULE TYPE: protein
10
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...393
20
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:
     Met Arg Lys Leu Phe Ile Pro Leu Leu Phe Ser Ala Leu Glu Ala
     Asn Glu Lys Asn Gly Phe Phe Ile Glu Ala Gly Phe Glu Thr Gly Leu
25
     Leu Glu Gly Thr Gln Thr Gln Glu Lys Arg His Thr Thr Thr Lys Asn
                                 40
     Thr Tyr Ala Thr Tyr Asn Tyr Leu Pro Thr Asp Thr Ile Leu Lys Arq
                             55
                                                 60
30
     Ala Ala Asn Leu Phe Thr Asn Ala Glu Ala Ile Ser Lys Leu Lys Phe
                         70
     Ser Ser Leu Ser Pro Val Arg Val Leu Tyr Met Tyr Asn Gly Gln Leu
                                         90
     Thr Ile Glu Asn Phe Leu Pro Tyr Asn Leu Asn Asn Val Lys Leu Ser
35
                                     105
     Phe Thr Asp Ala Gln Gly Asn Val Ile Asp Leu Gly Val Ile Glu Thr
                                 120
     Ile Pro Lys His Ser Lys Ile Val Leu Pro Gly Glu Ala Phe Asp Ser
                             135
     Leu Lys Ile Asp Pro Tyr Thr Leu Phe Leu Pro Lys Ile Glu Ala Thr
                         150
                                             155
     Ser Thr Ser Ile Ser Asp Ala Asn Thr Gln Arg Val Phe Glu Thr Leu
                                         170
     Asn Lys Ile Lys Thr Asn Leu Val Val Asn Tyr Arg Asn Glu Asn Lys
45
                                     185
     Phe Lys Asp His Glu Asn His Trp Glu Ala Phe Thr Pro Gln Thr Ala
                                 200
     Glu Glu Phe Thr Asn Leu Met Leu Asn Met Ile Ala Val Leu Asp Ser
                             215
50
     Gln Ser Trp Gly Asp Ala Ile Leu Asn Ala Pro Phe Glu Phe Thr Asn
                                             235
     Ser Pro Thr Asp Cys Asp Asn Asp Pro Ser Lys Cys Val Asn Pro Gly
                                        250
     Thr Asn Gly Leu Val Asn Ser Lys Val Asp Gln Lys Tyr Val Leu Asn
55
```

	гàз	GIII	275	me	vai	Asn	гÀ2	280	ьуs	Asn	Lys	Ala	Asp 285	Leu	Asp	Val
٠	Ile	Val 290		Lys	Asp	Ser	Gly 295		Val	Gly	Leu	Gly 300	Ser	Asp	Ile	Thr
5			Asn	Asn			Gly	Lys	His	Tyr		Gln	Leu	Gly	Val	Val
	305		: _	. •		310					315				-	320
					325					330					Lys 335	
10				340					345					350	His	
			355					360					365		Pro	
•	Thr	Lys 370	Asp	Gly	Gln	Val	Glu 375	Lys	Asp	Ser	Asn	Gly 380	Lys	Pro	Lys	Asp
15	Ser 385	Asp	Gly	Leu	Pro	Tyr 390	Asn	Val	Cys							
	(2)	INF	ORMA:	rion	FOR	SEQ	ID :	NO:84	4:							
20		(i)	) SE(	OUEN	CE CI	HARA	CTER	ISTI	CS:							
								mino		ds						
						ami										
						OGY:										
25		(ii	) MOI	LECUI	LE T	YPE:	pro	tein								
		(iii)	HYI	POTHI	ETIC	AL:	YES									
30		(vi)	OR													
30			(2	4) OI	(GAN	ISM:	Hel:	icoba	acte	r pyl	lori					
	•	(ix)	) FE	ו מוזיר '	7.											
		( +31,				KEY:	mis	c_fea	ature	•						
						CON :			ur	-						
			(1					6 <i>1</i> U								
35			(1	-, -				270							•	
35		(xi)	SEÇ		E DE	ESCR	IPTIC		SEQ I	ED NO	):84:	:				
35	Mot		SEÇ	UENC				ON: S								
35	Met 1		SEÇ	UENC				ON: S					Val	Leu	Ser	Ser
35	1	Lys	SEÇ	UEN(	Val 5	Ala	Leu	ON: S	Leu	Leu 10	Ser	Ala			15	
	1 Ser	Lys Leu	SE( Lys Leu	Phe Ala 20	Val 5 Glu	Ala Gly	Leu Asp	ON: S Gly Gly	Leu Val 25	Leu 10 Tyr	Ser Ile	Ala Gly	Thr	Asn 30	15 Tyr	Gln
	1 Ser	Lys Leu	SE( Lys Leu	Phe Ala 20	Val 5 Glu	Ala Gly	Leu Asp	ON: S Gly Gly	Leu Val 25	Leu 10 Tyr	Ser Ile	Ala Gly	Thr	Asn 30	15 Tyr	Gln
	1 Ser Leu	Lys Leu Gly	Lys Leu Gln 35	Phe Ala 20 Ala	Val 5 Glu Arg	Ala Gly Leu	Leu Asp Asn	Cly Gly Ser	Leu Val 25 Asn	Leu 10 Tyr	Ser Ile Tyr	Ala Gly Asn	Thr Thr 45	Asn 30 Gly	15 Tyr Asp	Gln Cys
40	1 Ser Leu	Lys Leu Gly Gly	Lys Leu Gln 35	Phe Ala 20 Ala	Val 5 Glu Arg	Ala Gly Leu	Leu Asp Asn Cys	Cly Gly Ser	Leu Val 25 Asn	Leu 10 Tyr	Ser Ile Tyr	Ala Gly Asn	Thr Thr 45	Asn 30 Gly	15 Tyr	Gln Cys
	Ser Leu Thr	Lys Leu Gly Gly 50	Lys Leu Gln 35 Ser	Phe Ala 20 Ala Val	Val 5 Glu Arg Val	Ala Gly Leu Gly	Leu Asp Asn Cys 55	Gly Gly Ser 40 Pro	Leu Val 25 Asn Pro	Leu 10 Tyr Ile Gly	Ser Ile Tyr Leu	Ala Gly Asn Thr	Thr Thr 45 Ala	Asn 30 Gly Asn	15 Tyr Asp Lys	Gln Cys His
40	Ser Leu Thr	Lys Leu Gly Gly 50	Lys Leu Gln 35 Ser	Phe Ala 20 Ala Val	Val 5 Glu Arg Val	Ala Gly Leu Gly Asn	Leu Asp Asn Cys 55	Gly Gly Ser 40 Pro	Leu Val 25 Asn Pro	Leu 10 Tyr Ile Gly	Ser Ile Tyr Leu Ser	Ala Gly Asn Thr	Thr Thr 45 Ala	Asn 30 Gly Asn	15 Tyr Asp	Gln Cys His
40	Ser Leu Thr Asn 65	Lys Leu Gly Gly 50 Pro	Lys Leu Gln 35 Ser	Phe Ala 20 Ala Val Gly	Val 5 Glu Arg Val	Ala Gly Leu Gly Asn 70	Asp Asn Cys 55 Ile	Gly Gly Ser 40 Pro	Leu Val 25 Asn Pro Trp	Leu 10 Tyr Ile Gly	Ser Ile Tyr Leu Ser 75	Ala Gly Asn Thr 60 Lys	Thr Thr 45 Ala Tyr	Asn 30 Gly Asn Ala	15 Tyr Asp Lys Asn	Gln Cys His Gly 80
40	Ser Leu Thr Asn 65	Lys Leu Gly Gly 50 Pro	Lys Leu Gln 35 Ser	Phe Ala 20 Ala Val Gly	Val 5 Glu Arg Val Thr	Ala Gly Leu Gly Asn 70	Asp Asn Cys 55 Ile	Gly Gly Ser 40 Pro	Leu Val 25 Asn Pro Trp	Leu 10 Tyr Ile Gly His	Ser Ile Tyr Leu Ser 75	Ala Gly Asn Thr 60 Lys	Thr Thr 45 Ala Tyr	Asn 30 Gly Asn Ala	15 Tyr Asp Lys Asn Phe	Gln Cys His Gly 80
40	Ser Leu Thr Asn 65 Ala	Lys Leu Gly Gly 50 Pro Leu	Lys Leu Gln 35 Ser Gly Asn	Phe Ala 20 Ala Val Gly	Val 5 Glu Arg Val Thr	Ala Gly Leu Gly Asn 70 Gly	Asp Asn Cys 55 Ile	Gly Gly Ser 40 Pro Asn	Leu Val 25 Asn Pro Trp	Leu 10 Tyr Ile Gly His Gly 90	Ser Ile Tyr Leu Ser 75	Ala Gly Asn Thr 60 Lys	Thr Thr 45 Ala Tyr Lys	Asn 30 Gly Asn Ala Phe	15 Tyr Asp Lys Asn Phe 95	Gln Cys His Gly 80 Gln
40	Ser Leu Thr Asn 65 Ala	Lys Leu Gly Gly 50 Pro Leu	Lys Leu Gln 35 Ser Gly Asn	Phe Ala 20 Ala Val Gly	Val 5 Glu Arg Val Thr	Ala Gly Leu Gly Asn 70 Gly	Asp Asn Cys 55 Ile	Gly Gly Ser 40 Pro Asn	Leu Val 25 Asn Pro Trp Val Lys	Leu 10 Tyr Ile Gly His Gly 90	Ser Ile Tyr Leu Ser 75	Ala Gly Asn Thr 60 Lys	Thr Thr 45 Ala Tyr Lys	Asn 30 Gly Asn Ala Phe	15 Tyr Asp Lys Asn Phe	Gln Cys His Gly 80 Gln
40	Ser Leu Thr Asn 65 Ala	Lys Leu Gly 50 Pro Leu Lys	Lys Leu Gln 35 Ser Gly Asn	Phe Ala 20 Ala Val Gly Gly Leu 100	Val 5 Glu Arg Val Thr Phe 85 Asp	Ala Gly Leu Gly Asn 70 Gly Met	Leu Asp Asn Cys 55 Ile Leu Thr	Gly Gly Ser 40 Pro Asn Asn Ser	Leu Val 25 Asn Pro Trp Val Lys 105	Leu 10 Tyr Ile Gly His Gly 90 Trp	Ser Ile Tyr Leu Ser 75 Tyr	Ala Gly Asn Thr 60 Lys Lys	Thr Thr 45 Ala Tyr Lys	Asn 30 Gly Asn Ala Phe Arg 110	15 Tyr Asp Lys Asn Phe 95 Val	Gln Cys His Gly 80 Gln Tyr
40	Ser Leu Thr Asn 65 Ala Phe	Lys Leu Gly Gly 50 Pro Leu Lys	Lys Leu Gln 35 Ser Gly Asn Ser	Phe Ala 20 Ala Val Gly Gly Leu 100 Asp	Val Sclu Arg Val Thr Phe 85 Asp	Ala Gly Leu Gly Asn 70 Gly Met	Leu Asp Asn Cys 55 Ile Leu Thr	Gly Gly Ser 40 Pro Asn Asn Ser Ala	Leu Val 25 Asn Pro Trp Val Lys 105 Asp	Leu 10 Tyr Ile Gly His Gly 90 Trp	Ser Ile Tyr Leu Ser 75 Tyr Phe	Ala Gly Asn Thr 60 Lys Lys Gly	Thr 45 Ala Tyr Lys Phe Gln 125	Asn 30 Gly Asn Ala Phe Arg 110 Val	15 Tyr Asp Lys Asn Phe 95 Val	Gln Cys His Gly 80 Gln Tyr
40	Ser Leu Thr Asn 65 Ala Phe	Lys Leu Gly Gly 50 Pro Leu Lys	Lys Leu Gln 35 Ser Gly Asn Ser	Phe Ala 20 Ala Val Gly Gly Leu 100 Asp	Val Sclu Arg Val Thr Phe 85 Asp	Ala Gly Leu Gly Asn 70 Gly Met	Leu Asp Asn Cys 55 Ile Leu Thr	Gly Gly Ser 40 Pro Asn Asn Ser Ala	Leu Val 25 Asn Pro Trp Val Lys 105 Asp	Leu 10 Tyr Ile Gly His Gly 90 Trp	Ser Ile Tyr Leu Ser 75 Tyr Phe	Ala Gly Asn Thr 60 Lys Lys Gly	Thr 45 Ala Tyr Lys Phe Gln 125	Asn 30 Gly Asn Ala Phe Arg 110 Val	15 Tyr Asp Lys Asn Phe 95 Val	Gln Cys His Gly 80 Gln Tyr

WO 98/18323 PCT/US97/19575

- 155 -

	Leu 145		Ala	Asp	Ile	Ile 150	Asp	Lys	Asp	Asn	Ala 155	Ser	Phe	Gly	Ile	Phe 160
			Val	Ala		Gly	Gly	Asn	Thr			Ser	Ser	Ala		
5	Tyr	Trp			165 Gln	Ile	Ile	Glu		170 Lys	Gly	Pro	Asp	•	175 Cys	Thr
	Dro	Th∽		180	Aan	Pro	A cm	<b>π</b> 1 -	185		C 0 m	mb.~	7.00	190	Com	mb v
	PIO	1111	195		Lai	FIO	ASII	200	PIO	ıyı	Ser	IIII	205	1111	Ser	1111
	Val	Ala	Phe	Gln	Val	Trp	Leu		Phe	Gly	Val	Arg		Asn	Ile	Tyr
10		210					215					220				•
		His	Asn	Gly	Val	Glu 230	Phe	Gly	Val	Arg		Pro	Leu	Leu	Ile	
	225 Lvs	Phe	Leu	Ser	Ala	Gly	Pro	Asn	Ala	Thr	235 Asn	Leu	Tvr	Tvr	His	240
	-1-				245				-	250			-1-	-1-	255	
15	Lys	Arg	Asp		Ser	Leu	Tyr	Leu	Gly	Tyr	Asn	Tyr	Thr	Phe		
	•			260					265			•		270		
	(2)	INF	ORMA:	rion	FOR	SEQ	ID I	NO : 8	5:							•
	,-,															
20		(i)		-		HARA										
				-		H: 14 ami			acio	ds						
						OGY:										
				, -												
25		(ii	) MOI	FECO	LE T	YPE:	prot	cein						•		
		1444	יעינו ו	וניייסח	om t Ci	AL: Y	vinc.									
		( + + + )	, AII	POIN	21161	. :بله	LES				•					
		(vi	OR	IGIN	AL S	OURCI	Ξ:									
30			(2	A) OI	RGAN	ISM:	Hel:	icoba	acte	r py:	lori					
		(iv	) FE	וסדזייי	·									•		
		. (				KEY:	misc	c fea	ature	2						
2.5						ON :		_								
35		423														•
		(X1)	SEG	<b>JOEN</b> (	JE DI	ESCR:	LPTIC	ON: S	SEQ .	LD NO	):85	:				
	Met	His	Pro	Ile	Met	Phe	Ala	Tyr	Ile	Ala	Asn	Ala	Leu	Ala	Gln	Ala
4.0	1				5					10				•	15	
40	Arg	Lys	Ile			Thr							_			Gln
	Val	Lvs	Glu			Ile								-		T.e.v
		-,,	35		<b>-</b> 1			40	- Lu	275		Deu	45	GLy	- TOIL	Deu
	Ser	Gln	Val	Ile	Ile	Tyr	Pro	Thr	Lys	Asp	Thr	Asp	Glu	Leu	Ile	Glu
45		50		_	_	_	55	_			_	60			_	
	Cys 65	GIA	vaı	Pro	Leu	Ser 70	Asp	ser	GIu	He	Asn 75	Phe	Leu	His	Asn	Thr 80
		Met	Arg	Ala	Arq	Gln	Val	Leu	Val	Lvs		Ile	Val	Thr	Asn	
	•				85					90			· · · · ·		95	
50	Ser	Ala	Phe		Glu	Ile	Asp	Leu		Lys	Ile	Cys	Lys		Tyr	Phe
	TIA	Dhe	T.e.v	100	הוה	Me+	Lev	V=1	105	<i>c</i> 1	T	C.~	C	110	T1.	T. 000
		FIIC	115	TTE	wra	Met	Ten	120	TT6	GIU	гуя	ser	125	MEL	тте	neu
	Lys	Lys		Thr	Lys	Lys	Leu		Arg	Lys	Ser	Ile				
55		130					135					140				

# (2) INFORMATION FOR SEQ ID NO:86:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 256 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein

10

- (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori

- (ix) FEATURE:
  - (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...256
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:
  - Met Leu Gly Ser Val Lys Lys Ala Val Phe Arg Val Leu Cys Leu Gly

    1 5 10
- Ala Leu Cys Leu Cys Gly Gly Leu Met Ala Glu Gln Asp Pro Lys Glu
- Leu Ile Phe Ser Gly Ile Thr Ile Tyr Thr Asp Lys Asn Phe Thr Arg
  - Ala Lys Lys Tyr Phe Glu Lys Ala Cys Lys Ser Asn Asp Ala Asp Gly
- Cys Ala Ile Leu Arg Glu Val Tyr Ser Ser Gly Lys Ala Ile Ala Arg
  65 70 75 80
  - Glu Asn Ala Arg Glu Ser Ile Glu Lys Ala Leu Glu His Thr Ala Thr
    85 90
- Ala Lys Val Cys Lys Leu Asn Asp Ala Glu Lys Cys Lys Asp Leu Ala
  100 105 110
  - Glu Phe Tyr Phe Asn Val Asn Asp Leu Lys Asn Ala Leu Glu Tyr Tyr
    115 120 125
  - Ser Lys Ser Cys Lys Leu Asn Asn Val Glu Gly Cys Met Leu Ser Ala 130 135 140
- Thr Phe Tyr Asn Asp Met Ile Lys Gly Leu Lys Lys Asp Lys Lys Asp 145 150 155 160
  - Leu Glu Tyr Tyr Ser Lys Ala Cys Glu Leu Asn Asn Gly Gly Gly Cys
    165 170 175
- Ser Lys Leu Gly Gly Asp Tyr Phe Phe Gly Glu Gly Val Thr Lys Asp
  180
  185
  190
  - Phe Lys Lys Ala Phe Glu Tyr Ser Ala Lys Ala Cys Glu Leu Asn Asp
    195 200 205
    Ala Lys Gly Cys Tyr Ala Lys Ala Lys Ala Lys Gly Cys Tyr Ala Lys Cys Tyr Cy
- Ala Lys Gly Cys Tyr Ala Leu Ala Ala Phe Tyr Asn Glu Gly Lys Gly
  210 215 220
- 50 Val Ala Lys Asp Glu Lys Gln Thr Thr Glu Asn Leu Glu Lys Ser Cys 225 230 235 240
  Lys Leu Gly Leu Lys Glu Ala Cys Asp Ile Leu Lys Glu Gln Lys Gln 245
- 55 (2) INFORMATION FOR SEQ ID NO:87:

```
(i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 242 amino acids
               (B) TYPE: amino acid
 5
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
        (iii) HYPOTHETICAL: YES
10
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
15
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...242
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:
20
     Met Lys Lys Phe Phe Ser Gln Ser Leu Leu Ala Leu Ile Ile Ser Met
                                         10
     Asn Ala Val Ser Gly Met Asp Gly Asn Gly Val Phe Leu Gly Ala Gly
                 20
                                     25
     Tyr Leu Gln Gly Gln Ala Gln Met His Ala Asp Ile Asn Ser Gln Lys
25
     Gln Ala Thr Asn Ala Thr Ile Lys Gly Phe Asp Ala Leu Leu Gly Tyr
     Gln Phe Phe Glu Lys His Phe Gly Leu Arg Leu Tyr Gly Phe Phe
                         70
30
     Asp Tyr Ala His Ala Asn Ser Ile Lys Leu Lys Asn Pro Asn Tyr Asn
                                         90
     Ser Glu Ala Ala Gln Val Ala Ser Gln Ile Leu Gly Lys Gln Glu Ile
                                     105
     Asn Arg Leu Thr Asn Ile Ala Asp Pro Arg Thr Phe Glu Pro Asn Met
35
                                 120
     Leu Thr Tyr Gly Gly Ala Met Asp Val Met Val Asn Val Ile Asn Asn
                            135
                                                 140
     Gly Ile Met Ser Leu Gly Ala Phe Gly Gly Ile Gln Leu Ala Gly Asn
                         150
                                             155
40
     Ser Trp Leu Met Ala Thr Pro Ser Phe Glu Gly Ile Leu Val Glu Gln
                    165
                                        170
     Ala Leu Val Ser Lys Lys Ala Thr Ser Phe Gln Phe Leu Phe Asn Val
                                     185
     Gly Ala Arg Leu Arg Ile Leu Lys His Ser Ser Ile Glu Ala Gly Val
45
                                200
     Lys Phe Pro Met Leu Lys Lys Asn Pro Tyr Ile Thr Ala Lys Asn Leu
                            215
                                              220
     Asp Ile Gly Phe Arg Arg Val Tyr Ser Trp Tyr Val Asn Tyr Val Phe
     225
                         230
```

- (2) INFORMATION FOR SEQ ID NO:88:
- 55 (i) SEQUENCE CHARACTERISTICS:

Thr Phe

```
(A) LENGTH: 267 amino acids
```

(B) TYPE: amino acid

(D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

10 (A) ORGANISM: Helicobacter pylori

(ix) FEATURE:

(A) NAME/KEY: misc\_feature

(B) LOCATION 1...267

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

Met Asn Tyr Pro Asn Leu Pro Asn Ser Ala Leu Glu Ile Ser Glu Gln 10 Pro Glu Val Lys Glu Ile Thr Asn Glu Leu Leu Lys Gln Leu Gln Asn 20 25 Ala Leu Arg Ser Asn Ala His Phe Ser Glu Gln Val Glu Leu Ser Leu 40 Lys Cys Ile Val Arg Ile Leu Glu Val Leu Leu Ser Leu Asp Phe Phe 25 55 Lys Asn Ala Asn Glu Ile Asp Ser Ser Leu Arg Asn Ser Ile Glu Trp . 70 Leu Thr Asn Ala Gly Glu Ser Leu Lys Leu Lys Met Lys Glu Tyr Glu 85 90 Arg Phe Phe Ser Glu Phe Asn Thr Ser Met His Ala Asn Glu Gln Glu 30 100 105 Val Thr Asn Thr Leu Asn Ala Asn Ala Glu Asn Ile Lys Ser Glu Ile 120 Lys Lys Leu Glu Asn Gln Leu Ile Glu Thr Thr Thr Arg Leu Leu Thr 35 135 Ser Tyr Gln Ile Phe Leu Asn Gln Ala Arg Asp Asn Ala Asn Asn Gln 150 155 Ile Thr Lys Asn Lys Thr Gln Ser Leu Glu Ala Ile Thr Gln Ala Lys 165 170 40 Asn Asn Ala Asn Asn Glu Ile Ser Asn Asn Gln Thr Gln Ala Ile Thr 185 Asn Ile Thr Glu Ala Lys Thr Asn Ala Asn Asn Glu Ile Ser Asn Asn 200 205 Gln Thr Gln Ala Ile Thr Asn Ile Asn Glu Ala Lys Glu Ser Ala Thr 45 215 220 Thr Gln Ile Asn Ala Asn Lys Gln Glu Ala Ile Asn Asn Ile Thr Gln 230 235 Glu Lys Thr Gln Ala Thr Ser Glu Ile Thr Glu Ala Lys Lys Thr Asp 245 50 His Tyr Gln Asn Ile Asp Phe Phe Glu Phe Glu

- (2) INFORMATION FOR SEQ ID NO:89:
- 55 (i) SEQUENCE CHARACTERISTICS:

```
(A) LENGTH: 544 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
10
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...544
15
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:
     Val Ile Glu Thr Ile Pro Lys His Ser Lys Ile Val Leu Pro Gly Glu
20
     Ala Phe Asp Ser Leu Lys Glu Ala Phe Asp Lys Ile Asp Pro Tyr Thr
     Phe Phe Phe Pro Lys Phe Glu Ala Thr Ser Thr Ser Ile Ser Asp Thr
                                 40
     Asn Thr Gln Arg Val Phe Glu Thr Leu Asn Asn Ile Lys Thr Asn Leu
25
                             55
     Ile Met Lys Tyr Ser Asn Glu Asn Pro Asn Asn Phe Asn Thr Cys Pro
                         70
                                            75
     Tyr Asn Asn Asn Gly Asn Thr Lys Asn Asp Cys Trp Gln Asn Phe Thr
                  85
                                         90
30
     Pro Gln Thr Ala Glu Glu Phe Thr Asn Leu Met Leu Asn Met Ile Ala
                                     105
     Val Leu Asp Ser Gln Ser Trp Gly Asp Ala Ile Leu Asn Ala Pro Phe
                                 120
     Glu Phe Thr Asn Ser Ser Thr Asp Cys Asp Ser Asp Pro Ser Lys Cys
35
                             135
     Val Asn Pro Gly Val Asn Gly Arg Val Asp Thr Lys Val Asp Gln Gln
                         150
     Tyr Ile Leu Asn Lys Gln Gly Ile Ile Asn Asn Phe Arg Lys Lys Ile
                                         170
     Glu Ile Asp Ala Val Val Leu Lys Asn Ser Gly Val Val Gly Leu Ala
                                    185
     Asn Gly Tyr Gly Asn Asp Gly Glu Tyr Gly Thr Leu Gly Val Glu Ala
                                 200
     Tyr Ala Leu Asp Pro Lys Lys Leu Phe Gly Asn Asp Leu Lys Thr Ile
45
                             215
    Asn Leu Glu Asp Leu Arg Thr Ile Leu His Glu Phe Ser His Thr Lys
                         230
                                             235
    Gly Tyr Gly His Asn Gly Asn Met Thr Tyr Gln Arg Val Pro Val Thr
                    245
                                         250
    Lys Asp Gly Gln Val Glu Lys Asp Ser Asn Gly Lys Pro Lys Asp Ser
                                     265
    Asp Gly Leu Pro Tyr Asn Val Cys Ser Leu Tyr Gly Gly Ser Asn Gln
                                280
    Pro Ala Phe Pro Ser Asn Tyr Pro Asn Ser Ile Tyr His Asn Cys Ala
55
                                                .300
```

	Asp	Val	Pro	Ala	Gly		Leu	Gly	Val	Thr		Ala	Val	Trp	Gln	Gln
			Asn	Gln		310 Ala	Leu	Pro	Ile	Asn	315 Tyr	Ala	Asn	Leu	Gly	320 Ser
5	Gln	Th*	λcn	Тагас	325	7 011	3	27-	0	330	_			_	335	
				340				*	345					350		Ala
			355					360					365			Val
10	Thr	Asn 370	His	His	Phe	Ser	Asn 375	Ala	Ser	Gln	Ser	Phe 380		Ser	Pro	Ile
	Leu 385	Gly	Val	Asn	Ala	Lys 390	Ile	Gly	Tyr	Gln	Asn 395			Asn	Asp	Phe
		Gly	Leu	Ala	Tyr 405		Gly	Ile	Ile			Asn	Tyr	Ala		400 Ala
15	Val	Asn	Gln	Lys	Val	Gln	Gln	Leu		410 Tyr	Gly	Gly	Gly	Ile	415 Asp	Leu
	Leu	Leu	Asp	420 Phe		Thr	Thr	Tyr	425 Ser	Asn	Lys	Asn	Ser	430 Pro	Thr	Gly
			435					440				٠.	445			Gly
20		450					455					460		Val		
-	465					470					475					480
25					485					490				Tyr	495	
25				500					505					Arg 510		
			<b>51</b> 5					520					525	Val		
30	Glu	Gly 530	Ala	Ser	His	Phe	Lys 535	Val	Phe	Phe	Asn	Tyr 540	Gly	Gly	Cys	Phe
	(2)	INFO	RMAT	CION	FOR	SEQ	ID N	iO:90	) <u>:</u>							
		(i)	SEC	UENC	E CH	IARAC	TERI	STIC	:S :							
35			(2	) LE	NGTH	l: 35	6 am	ino		ls						
						GY:										
40		(ii)	MOL	ECUL	E TY	PE:	prot	ein				. ,				
	(	iii)	HYP	OTHE	TICA	L: Y	ES									
		(vi)	ORI	GINA	L SO	URCE	:									
45 ·			A)	) OR	GANI	SM:	Heli	coba	cter	pyl	ori	,				
		(ix)	FEA					£				:				
						EY: ON 1			cure							
50		(xi)	SEQ	UENC	E DE	SCRI	PTIO	N: S	EQ I	D NO	:90:					
	Leu	Met	Lys			Leu	Leu	Phe	Met	Ile	Phe	Val	Val	Cys	Gln	Leu
	1 Glu				5					10					15	
55				20					25				_	30		

	Tyr	Leu	Arg 35	Lys	Gln	Asp	Leu	His 40	Ile	Ile	Lys	Thr	Gln 45	Asn	Asp	Leu
		50					55					60				Ser
5	65					Lys 70					75					80
					85	Phe				90					95	_
10				100		Asn			105					110		
			115			Pro		120					125		_	<u> </u>
15		130				Tyr	135					140			_	٠.
15		Pro	GIn	Ser	Ala	Pro		Arg	Met	Ile		Phe	Met	Pro	Glu	
	145	<b></b>	**- 1	m	D	150			_·.		155			<u>.</u>	_	160
•					165	Ile				170	-				175	
20				180		Trp			185					190		
			195			Tyr		200					205			
25		210				Gln	215					220				
25	225					Gly 230					235					240
					245	Val				250					255	
30				260		Val			265					270		
			275			Gly		280					285			
35		290				Gln	295					300				
55	305	•				Gly 310					315					320
					325	Ile				330					335	
40	Gly	Leu	Tyr	Glu 340	Tyr	Asp	Val	Phe	Ser 345	Asn	Arg	Ile	Gly	Val 350	Gly	Ile
	Arg	Leu	Asn 355	Pro												

(2) INFORMATION FOR SEQ ID NO:91:

45

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 675 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- 55 (vi) ORIGINAL SOURCE:

## (A) ORGANISM: Helicobacter pylori

### (ix) FEATURE:

- (A) NAME/KEY: misc\_feature (B) LOCATION 1...675

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

10	1				5					10					15	Ala
				20					25					30	•	Ser
			35			*		40			Leu		45			
15		50					55					60				
	65					.70	*				Leu 75					80
20					85					90	Phe				95	
-				100					105		Asp			110		
25			115					120			Lys		125			
25		130					135				Ala	140				
	145					150					Met 155					160
30					165					170	Phe				175	
٠				180				-	185		Ser			190		
35			195					200			Phe		205			
<i>J J</i>		210					215				Leu	220				
	225					230					Thr 235					240
40					245					250	Glu				255	
				260					265		Thr			270		_
45			275					280			Met		285			
		290					295				Ser	300				
•	305					310					Leu 315					320
50					325					330	Leu				335	
				340					345		Asn			350		
55			355					360			Asp		365			
	GTII	T 11T	wra	TTG	ASI1	пλя	ASII	тте	ьeu	GIn	Thr	Gln	Lys	Thr	Met	Gln

(ix) FEATURE:

	370					375					380				
Glu	Asp	Arg	Gln	Ala	Val	Gln	Asp	Thr	Ile	Lys	Val	Val	Ser	Asp	Val
- 385		_			390					395					400
Lys	Ala	Gly	Asn		Ala	Val	Arg	Ile		Ala	Glu	Pro	Ala		Pro
<b>3</b>		7	<b>a</b> 1		3			-		~->			_		
			420					425					430	_	
		435					440					445			
Ser	Tyr 450	Ser	Gly	Leu	Asp	Phe 455	Arg	Gly	Arg	Ile	Gln 460	Asn	Ala	Ser	Gly
Arg 465	Val	Glu	Leu	Val	Thr 470	Asn	Ala	Leu	Gly		Glu	Ile	Gln	Lys	Met 480
Leu	Glu	Thr	Ser	Ser 485	Asn	Phe	Ala	Lys			Ala	Asn	Asp		
Asn	Leu	Lys		Cys	Val	Gln	Asn			Lys	Ala	Ser			Gln
His	Lys			Met	Glu	Thr			Thr	Ile	Glu			Thr	Thr
Ser			Gly	Val	Ser			Ser	Glu	Ala			Glu	Gln	Gly
		Ile	Lys	Ser			Glu	Ile	Ile			Ile	Ala	Asp	
	Asn	Leu	Leu			Asn	Ala	Ala			Ala	Ala	Arg	Ala	560 Gly
Glu	His				Phe	Ala	Val			Asp	Glu	Val	Arg	575 Lys	Leu
Ala	Glu			Gln	Lys	Ser	Leu	585 Ser	Glu	Ile	Glu	Ala	590 Asn	Ile	Asn
Ile	Leu		Gln	Ser	Ile	Ser	600 Asp	Thr	Ser	Glu	Ser	605 Ile	Lys	Asn	Gln
Val	610 Lys	Glu	Val	Glu	Glu	615 Ile	Asn	Ala	Ser	Ile	620 Glu	Ala	Leu	Arg	Ser
625					630					635					640
				645					650			•		655	
Gln	Glu	Ile	Asp 660	Lys	Val	Ser	Asn	Asp 665	Ile	Leu	Glu	Asp	Val 670	Asn	Lys
Lys	Gln														٠,
(0)				DOD.	270										
(2)															
	(i)	(F	) LE	NGTI	I: 27	71 an	nino		ls	-			-		
											-				
	(ii)	MOI	ECUI	E TY	PE:	prot	ein								
. (	(iii)	HYE	РОТНЕ	ETIC#	L: Y	ES									
	(vi)	ORI	GINA	L SC	URCE	:									
	Asp Gln Ser Arg 465 Leu Asn His Ser Lys 545 Thr Glu Ala Ile Val 625 Val Gln Lys (2)	Glu Asp 385 Lys Ala Asp Leu Gln Glu Ser Tyr 450 Arg Val 465 Leu Glu Asn Leu His Lys Ser Ile 530 Lys Asp 545 Thr Asn Glu His Ala Glu Ile Leu 610 Val Lys 625 Val Thr Gln Glu Lys Gln (2) INFO (ii) (iii)	Glu Asp Arg 385 Lys Ala Gly Asp Leu Lys Gln Glu Ser 435 Ser Tyr Ser 450 Arg Val Glu 465 Leu Glu Thr Asn Leu Lys His Lys Ser 515 Ser Ile Gln 530 Lys Asp Ile 545 Thr Asn Leu Glu His Gly Ala Glu Arg 595 Ile Leu Val 610 Val Lys Glu 625 Val Thr Glu Gln Glu Ile Lys Gln Phe 675 (2) INFORMAT (i) SEG (ii) MOI (iii) MOI	Glu Asp Arg Gln 385 Lys Ala Gly Asn Asp Leu Lys Glu 420 Gln Glu Ser Val 435 Ser Tyr Ser Gly 450 Arg Val Glu Leu 465 Leu Glu Thr Ser Asn Leu Lys Glu 500 His Lys Ser Leu 515 Ser Ile Gln Gly 530 Lys Asp Ile Lys 545 Thr Asn Leu Leu Glu His Gly Arg 580 Ala Glu Arg Thr 595 Ile Leu Val Gln 610 Val Lys Glu Val 625 Val Thr Glu Gly Gln Glu Ile Asp 660 Lys Gln Phe 675  (2) INFORMATION  (i) SEQUENC (A) LE (B) TY (D) TO  (ii) MOLECUI	Glu Asp Arg Gln Ala  385  Lys Ala Gly Asn Phe  405  Asp Leu Lys Glu Leu 420  Gln Glu Ser Val Gly 435  Ser Tyr Ser Gly Leu 450  Arg Val Glu Leu Val 465  Leu Glu Thr Ser Ser 485  Asn Leu Lys Glu Cys 500  His Lys Ser Leu Met 515  Ser Ile Gln Gly Val 530  Lys Asp Ile Lys Ser 545  Thr Asn Leu Leu Ala 565  Glu His Gly Arg Gly 580  Ala Glu Arg Thr Gln 595  Ile Leu Val Gln Ser 610  Val Lys Glu Val Glu 625  Val Thr Glu Gly Asn 645  Gln Glu Ile Asp Lys 660  Lys Gln Phe 675  (i) SEQUENCE Cr (A) LENGTE (B) TYPE: (D) TOPOLO  (ii) MOLECULE TY (iii) MOLECULE TY	Glu Asp Arg Gln Ala Val 385 390  Lys Ala Gly Asn Phe Ala 405  Asp Leu Lys Glu Leu Arg 420  Gln Glu Ser Val Gly Thr 435  Ser Tyr Ser Gly Leu Asp 450  Arg Val Glu Leu Val Thr 465 470  Leu Glu Thr Ser Ser Asn 485  Asn Leu Lys Glu Cys Val 500  His Lys Ser Leu Met Glu 515  Ser Ile Gln Gly Val Ser 530  Lys Asp Ile Lys Ser Ile 545  Thr Asn Leu Leu Ala Leu 565  Glu His Gly Arg Gly Phe 580  Ala Glu Arg Thr Gln Lys 595  Ile Leu Val Gln Ser Ile 610  Val Lys Glu Val Glu Glu 625 630  Val Thr Glu Gly Asn Leu 645  Gln Glu Ile Asp Lys Val 660  Lys Gln Phe 675  (2) INFORMATION FOR SEQ (i) SEQUENCE CHARAC (A) LENGTH: 27 (B) TYPE: amin (D) TOPOLOGY:  (iii) MOLECULE TYPE:	Glu Asp Arg Gln Ala Val Gln  385	Glu Asp Arg Gln Ala Val Gln Asp 385   390	Glu Asp Arg Gln Ala Val Gln Asp Thr 385   390	Glu Asp Arg Gln Ala   Val Gln Asp Thr Ile   390	Glu Asp Arg Gln Ala Val Gln Asp Thr Ile Lys 385	Glu Asp Arg Gln Ala   Val Gln Asp Thr Ile Lys Val 385   390   395	Glu Asp Arg Gln Ala Val Gln Asp Thr Ile Lys Val Val 385   390   395	Glu Asp Arg Gln Ala Val Gln Asp Thr Ile Lys Val Val Ser 395	Glu Asp Arg Gln Ala Val Gln Asp Thr Ile Lys Val Val Ser Asp 385   390   395   395   395   395   395   396

- (A) NAME/KEY: misc feature
- (B) LOCATION 1...271
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:
- Met Asn Ile Phe Lys Arg Ile Ile Cys Val Thr Ala Ile Val Leu Gly Phe Phe Asn Leu Leu Asp Ala Lys His His Lys Glu Lys Lys Glu Asp

- His Lys Ile Thr Arg Glu Leu Lys Val Gly Ala Asn Pro Val Pro His
  - Ala Gln Ile Leu Gln Ser Val Val Asp Asp Leu Lys Glu Lys Gly Ile
- Lys Leu Val Ile Val Ser Phe Thr Asp Tyr Val Leu Pro Asn Leu Ala 15 75 Leu Asn Asp Gly Ser Leu Asp Ala Asn Tyr Phe Gln His Arg Pro Tyr
  - 90 Leu Asp Arg Phe Asn Leu Asp Arg Lys Met His Leu Val Gly Leu Ala
- 100 105 20 Asn Ile His Val Glu Pro Leu Arg Phe Tyr Ser Gln Lys Ile Thr Asp
  - 120 Ile Lys Asn Leu Lys Lys Gly Ser Val Ile Ala Val Pro Asn Asp Pro 135
- Ala Asn Gln Gly Arg Ala Leu Ile Leu Leu His Lys Gln Gly Leu Ile 25 150 155
  - Ala Leu Lys Asp Pro Ser Asn Leu Tyr Ala Thr Glu Phe Asp Ile Val 170
  - Lys Asn Pro Tyr Asn Ile Lys Ile Lys Pro Leu Glu Ala Ala Leu Leu 185
- 30 Pro Lys Val Leu Gly Asp Val Asp Gly Ala Ile Ile Thr Gly Asn Tyr 200
  - Ala Leu Gln Ala Lys Leu Thr Gly Ala Leu Phe Ser Glu Asp Lys Asp 215
- Ser Pro Tyr Ala Asn Leu Val Ala Ser Arg Glu Asp Asn Ala Gln Asp 230 235
  - Glu Ala Ile Lys Ala Leu Ile Glu Ala Leu Gln Ser Glu Lys Thr Arg 250
- Lys Phe Ile Leu Asp Thr Tyr Lys Gly Ala Ile Ile Pro Ala Phe 40
  - (2) INFORMATION FOR SEQ ID NO:93:
    - (i) SEQUENCE CHARACTERISTICS:
      - (A) LENGTH: 161 amino acids
      - (B) TYPE: amino acid
        - (D) TOPOLOGY: linear
    - (ii) MOLECULE TYPE: protein
- 50 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
- 55 (ix) FEATURE:

```
(A) NAME/KEY: misc_feature
```

(B) LOCATION 1...161

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

Met Phe Phe Lys Thr Tyr Gln Lys Leu Leu Gly Ala Ser Cys Leu Ala Leu Tyr Leu Val Gly Cys Gly Asn Gly Gly Gly Glu Ser Pro Val Glu Met Ile Ala Asn Ser Glu Gly Thr Phe Gln Ile Asp Ser Lys Ala 10 Asp Ser Ile Thr Ile Gln Gly Val Lys Leu Asn Arg Gly Asn Cys Ala Val Asn Phe Val Pro Val Ser Glu Thr Phe Gln Met Gly Val Leu Ser 15 Gln Val Thr Pro Ile Ser Ile Gln Asp Phe Lys Asp Met Ala Ser Thr 90 Tyr Lys Ile Phe Asp Gln Lys Lys Gly Leu Ala Asn Ile Ala Asn Lys 105 20 Ile Ser Gln Leu Glu Gln Lys Gly Val Met Met Glu Pro Gln Thr Leu 120 Asn Phe Gly Glu Ser Leu Lys Gly Ile Ser Gln Gly Cys Asn Ile Ile 135 140 Glu Ala Glu Ile Gln Thr Asp Lys Gly Ala Trp Thr Phe Asn Phe Asp 25 150 155

(2) INFORMATION FOR SEQ ID NO:94:

30

Lys

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 337 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- 40 (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc feature
- 45 (B) LOCATION 1...337
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

		EΛ															
	T 011	50	0	- G1		_	55	_				60					
	65					70					75					Arg 80	
- 5	Glu	Lys	Ile	Phe	Glu 85	Cys	Val	Glu	Glu	Glu 90	Lys	His	Lys	Gln	Ala 95	Leu	
	Asn	Leu	Ile	Asn 100	Lys	Glu	Asp	Thr	Glu 105	Asp	Lys	Glu	Glu		Ala	Lys	
	Lys	Ile	Lys 115	Glu		Lys	Glu	Lys			Val	Leu		110 Gln	Lys	Phe	
10	Met	Ala	Phe		Met	Lys	Glu	120 His	Ser	Lys	Glu	Phe	125 Pro	Asn	Lys	Lys	
	Gln	130 Leu	Gln	Thr	Met	Leu	135 Glu	Asn	Ala	Phe	Asp	140 Asn	Gly	Ala	Glu	Ser	
	145					150					155					160	
15	*		Asp		165					170					175		
ř			Lys	180					185					190	Lys		
	Leu	Ala	Phe 195	Gly	Glu	Arg	Ser	Tyr 200	Ile	Arg	Gln	Tyr	Lys 205	Lys	Asp	Phe	
20	Glu	Glu 210	Ser	Thr	Tyr	Asp	Thr 215	Arg	Gln	Thr	Leu	Ser 220	Ala	Met	Ala	Asn	
	Met 225	Ser	Gly	Glu	Asn	Asp 230	Tyr	Lys	Ile	Thr	Trp 235	Leu	Lys	Pro	Lys	Tyr 240	
25	Gln	Leu	His	Ser	Ser 245	Asn	Asn	Ile	Lys	Pro 250	Leu	Met	Ser	Asn	Thr 255	Glu	
	Leu	Leu	Asn	Met 260	Ile	Glu	Leu	Thr	Asn 265	Ile	Lys	Lys	Glu	Tyr 270	Val	Met	
	Gly	Cys	Asn 275	Met	Glu	Ile	Asp	Gly 280	Ser	Lys	Tyr	Pro	Ile 285	His	Lys	Asp	
30	Trp	Gly 290	Phe	Phe	Gly	Lys	Ala 295		Val	Pro	Glu	Thr	Trp	Arg	Asn	Lys	
•	Ile 305	Trp	Glu	Cys	Ile	Lys		Lys	Val	Lys		Tyr	Asp	Asn	Thr	Thr	
		C1.,	T1.0	a1	T1 -	310		_	_		315					320	
35		GIU	Ile	GIY	325	val	Trp	гуѕ	Lys	Asn 330	Thr	Tyr	Ser	Ile	Ser 335	His	
	His											*					
40	(2)	INFO	RMAT	ION	FOR	SEQ	ID N	iO: 95	:			,					
40		421	-														
	1	(1)	SEC														
	. *							ino	acid	s							
						amin GY:					•						
45			(1)	, 10	POLIC	GI:	TIHE	ar									
	•	(ii)	MOL	ECUL	E TY	PE:	prot	ein							•		
	. (	iii)	HYP	OTHE	TICA	L: Y	ES										
50		(vi)	ORI (A					coba	cter	pyl	ori						
		(ix)	FEA			<b>-</b>	•	_									
55						EY: 1 ON 1		_fea 16	ture								

(B) LOCATION 1...416

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

5	Met 1	Lys	Lys	Leu	Val 5	Phe	Ser	Met	Leu	Leu 10	Cys	Cys	Lys	Ser	Val 15	Phe
	Ala	Glu	Gly	Glu 20	Thr	Pro	Leu	Ile	Val 25	Asn	Asp	Pro	Glu	Thr 30	His	Val
	Ser	Gln	Ala 35	Thr	Ile	Ile	Gly	Lys 40	Met	Val	Asp	Ser	Ile 45	Lys	Arg	Tyr
10	Glu	Glu 50	Ile	Ile	Ser	Lys	Ala 55	Gln	Ala	Gln	Val	Asn 60	Gln	Leu	Gln	Lys
	Val 65	Asn	Asn	Met	Ile	Asn 70	Thr	Thr	Asn	Ser	Leu 75	Ile	Ser	Ser	Ser	Ala 80
15	Ile	Thr	Leu	Ala	Asn 85	Pro	Met	Gln	Val	Leu 90	Gln	Asn	Ala	Gln	Tyr 95	Gln
٠.				100					105					110		
			115					120		Asn			125			
20		130					135			Thr		140				
	145					150				Lys	155	_		•		160
25					165					Gln 170				_	175	_
	_			180					185	Glu			_	190		_
20			195					200		Asp			205			
30	•	210					215			Pro		220		•	-	
•	225					230				Asn	235		-			240
35				_	245				_	Leu 250					255	
				260					265	His		_		270		
40			275					280		Lys			285			
70		290					295			Ser		300				
	305	Deu	1111	Deu	Asp	310	116	Буз	AIG	Ser	315	пуs	Asp	MIA.	GIII	320
45	Gln	Ala	Tyr	Ala	Asn 325	Phe	Asn	Gln	Arg	Ile 330	Lys	Leu	Leu	Thr	Leu 335	Lys
	Tyr	Leu	Lys	Glu 340		Thr	Asn	Gln	Met 345	Leu	Phe	Leu	Asn	Gln 350		Met
	Ala	Met	Gln 355	Ser	Glu	Ile	Met	Thr 360	Asp	Asp	Tyr	Phe	Arg 365		Asn	Asn
50	Asp	Gly 370	Phe	Gly	Glu	Lys	Glu 375	Asn	His	Ile	Asp	Lys 380	Gln	Leu	Thr	Gln
	Lys 385	Arg	Ile	Asn	Glu	Arg 390	Glu	Arg	Ala	Arg	Ile 395	Tyr	Phe	Gln	Asn	Pro 400
55	Asn	Val	Lys	Phe	Asp 405	Gln	Phe	Gly	Phe	Pro 410	Ile	Phe	Ser	·Ile	Trp 415	Asp

```
(2) INFORMATION FOR SEQ ID NO:96:
```

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 376 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

10

5

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

15

55

(ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...376
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

Val Asn Lys Trp Ile Lys Gly Ala Val Val Phe Val Gly Gly Phe Ala Thr Ile Thr Thr Phe Ser Leu Ile Tyr His Gln Lys Pro Lys Ala Pro 25 Leu Asn Asn Gln Pro Ser Leu Leu Asn Asp Asp Glu Val Lys Tyr Pro 40 Leu Gln Asp Tyr Thr Phe Thr Gln Asn Pro Gln Pro Thr Asn Thr Glu 55 30 Ser Ser Lys Asp Ala Thr Ile Lys Ala Leu Gln Glu Gln Leu Lys Ala 70 75 Ala Leu Lys Ala Leu Asn Ser Lys Glu Met Asn Tyr Ser Lys Glu Glu 85 90 Thr Phe Thr Ser Pro Pro Met Asp Pro Lys Thr Thr Pro Pro Lys Lys 35 100 105 Asp Phe Ser Pro Lys Gln Leu Asp Leu Leu Ala Ser Arg Ile Thr Pro 115 120 Phe Lys Gln Ser Pro Lys Asn Tyr Glu Glu Asn Leu Ile Phe Pro Val 135 40 Asp Asn Pro Asn Gly Ile Asp Ser Phe Thr Asn Leu Lys Glu Lys Asp 150 Ile Ala Thr Asn Glu Asn Lys Leu Leu Arg Thr Ile Thr Ala Asp Lys 165 170 Met Ile Pro Ala Phe Leu Ile Thr Pro Ile Ser Ser Gln Ile Ala Gly 185 Lys Val Ile Ala Gln Val Glu Ser Asp Ile Phe Ala Ser Met Gly Lys 200 Ala Val Leu Ile Pro Lys Gly Ser Lys Val Ile Gly Tyr Tyr Ser Asn 215 50 Asn Asn Lys Met Gly Glu Tyr Arg Leu Asp Ile Val Trp Ser Arg Ile 230 235 Ile Thr Pro His Gly Ile Asn Ile Met Leu Thr Asn Ala Lys Gly Ala 245 250 Asp Ile Lys Gly Tyr Asn Gly Leu Val Gly Glu Leu Ile Glu Arg Asn

PCT/US97/19575

	Phe	Gln	Arg 275	Tyr	Gly	Val	Pro	Leu 280	Leu	Leu	Ser	Thr	Leu 285	Thr	Asn	Gly
	Leu	Leu 290	Ile	Gly	Ile	Thr	Ser 295	Ala	Leu	Asn	Asn	Arg	Gly	Asn	Lys	Glu
5	Glu	Val	Thr	Asn	Phe	Phe	Gly	Asp	Tyr	Leu	Leu	Leu	${\tt Gln}$	Leu	Met	Arg
	305	_			01	310	<b>&gt;</b>	<b>~</b> 1	**- 7	**- *	315	<b>61.</b>	<b>71</b>	T	3	320
	GIN	ser	GIY	Met.	325	iie	ASI	GIN	vai	330	ASII	GIN	ire		335	Asp
10	Lys	Ser	Lys	Ile 340		Pro	Ile	Val	Val 345		Arg	Glu	Gly ·			Val
	Phe	Ile	Ser 355	Pro	Asn	Thr		Ile 360	Phe	Phe	Pro	Ile	Pro 365	Arg	Glu	Asn
	Glu	Val	Ile	Ala	Glu	Phe	Leu	Lys								
15		370					375									
15	(2)	TNF	ORMA'	TION	FOR	SEO	ID 1	10:9	7 :							
	\-,								. •							
		(i)		QUEN						_						
20			-	A) LI B) Ti					acı	15						
20				D) T							•					
		(ii)	) MOI	LECUI	LE T	YPE:	prot	cein			. •					
25	-	(iii)	HY	РОТНІ	ETIC	AL: ?	YES									
		(vi)	OR:	IGIN	AL S	OURCI	Ξ:									
			1 (2	A) OI	RGAN:	ISM:	Hel:	icob	acte	г ру	lori					
30		/i~	) FF:	ATURI												
30		(12,		A) N		KEY:	mis	c fea	ature	<u> </u>						
			· (1	B) L	OCAT:	ION :	1	916								
		124	\ CE	QUEN	ירו שי	בפרים.	TDTT	N	SEO .	או בו	1.97					
35		(XI,	, SE	SOEM.	יע פיי	SOCK.	IP I I	JN : .	SEQ.	LD M	J. <del>J</del> /	•				
	Val	Asp	Leu	Arg	Ile	Gln	Ser	Lys	Glu	Val	Ser	His	Asn	Leu	Lys	Glu
	1 .	<b>9</b>	T	mb	.5	T1.		· ·	D	10 Db.	<b>63</b>	T	17-	17-1	15	. "
	Leu	ser	гуя	Thr 20	Leu	TIE	ser	Tyr	25	Pne	GIU	ьys	HIS	30	GTU	MIA
40	Leu	Gly	Glu	Gln	Cys	Ser	Asn	Phe	Val	Ser	Ile	Pro	Ile	Asn	Asn	Asp
		<b>m</b>	35	3	T1.		mb	40	11-1	C	3	Dh.	45 T10	7	T 033	T10
	qea	1yr 50	ser	Asn	IIe	Cys	55	Phe	vai	ser	Asp	o o	me	ASII	ren	TTE
	Ala		Tyr	Asn	Leu	Leu		Ser	Phe	Leu	Asp		Tyr	Lys	Asp	Lys
45	65		_	•		70	• ,				75					80
	Leu	Lys	Leu	Ser		Leu	Val	Thr	Glu		Ala	Asn	Val	Thr		Asn
	Len	Leu	Phe	Lys	85 Lvs	Leu	Ile	Lvs	His	90 Leu	Ser	Glv	Asn	Asn	95 Gln	Leu
				100				_,, 5	105			1		110		
50	Val	Lys		Phe	Tyr	Gln	Cys		Arg	Glu	Ile	Ile		Tyr	Asn	Ala
	Dwa	700	115	Glu	ጥታ	Tare	Dro	120	G] n	Dhe	Dhe	Tle	125	Glv	Lve	Glv
	PLO	130	пåа	GIU	TÄT	nys	135	uali	3711	FIIC	5.116	140	116	ΨŦΫ	درد	O± y
	Lys		Lys	Gln	Leu			Ile	Tyr	Ser	His		Lys	Glu	Leu	
55	145					150					155					160

٠.	Ala	Ser	Glu	Ile	Lys 165	Pro	Gln	Asp	Met	Glu 170	Asp	Ile	Leu	Lys	Lys 175	Leu
	Glu	Glu	Leu	Asp 180	Lys	Ile	Phe	Lys	Thr 185	Thr	Asp	Phe	Thr	Lys 190	Phe	Thr
5	Pro	Lys	Thr 195	Glu	Ile	Lys	Asp	Ile 200		Lys	Glu	Ile	Asp	Glu	Lys	Tyr
	Pro	Ile 210		Glu	Asn	Phe	Lys 215			Phe	Asn	Glu 220		Glu	Ser	Asn
10	Ile 225		Lys	His	Asp	Glu 230		Lys	Lys	Asp	Phe 235		Arg	Asn	Lys	Glu
••		Leu	Ile	Arq	Glu		Glu	Asn	His	Cvs		Asn	Glu	Cys	Δen	240 Ser
					245					250					255	
1.5				260					265					Asn 270		
15			275					280					285	Asp		
	Lys	Asp 290	Ile	Lys	Ser	Met	Met 295	Cys	Gln	Phe	Tyr	Leu 300	Lys	Gln	Ile	Asp
	Leu	Leu	Val	Asn	Ser	Glu	Ile	Val	Arg	Tyr	Arg	Tyr	Ser	Asn	Leu	Phe
20	305	_			_	310	_				315					320
					325					330				Leu	335	
	Glu	Ser	Gly		Tyr	Leu	Phe	Pro		Asn	Ile	Gly	Glu	Ile	Lys	Asp
25	Taré	Dhe	Gl n	340	λαη	Laze	G1.,	Taro	345	T	<b>71</b>	G		350 Asn	**- 7	<b>~</b>
			355					360					365			
		370					375					380		Ala		
30		His	Leu	Asn	Ile		Asn	Gly	Leu	Ser		Gln	Phe	Glu		
30	385 Val	Pro	Tle	Met	Lvs	390 Glu	Туг	Lare	Glu	Dro	395	T1.	The	Asp		400
					405					410					415	
35				420					425					Gln 430		
			435					440					445	Asn		
		450					455					460		Ser	_	
40		Phe	Asp	Lys	Ąsp		Glu	Ile	Tyr	Phe	Asp	Ser	His	Glu	Ser	Phe
40	465	Tla	Co**	7	T	470	T	a1-	a2	-7	475	<b>~</b> 7		_	_	480
				. "	485					490				Ser	495	
	гуѕ	TTE	гÀ2	500	ser	rys	Asp	Phe		Ser	Ile	Gln	Lys		Glu	Ser
45	Lys	His			Asn	Asp	Iļe		505 Gln	Leu	Glu	Phe		510 Glu	Asn	Asp
	Thr	Ser	515 Phe	Leu	Phe	Ala	Lys	520 Gly	Ser	Phe	Ala	Glu	525 Ile	Leu	Glu	Tyr
	7	530	<b>~</b> 1	T	• -	-1	535		_			540				
50	Asn 545	met	GIN	ren	гàг	550	Asp	Ser	Leu	Ile		Lys	Glu	Phe	Asn	
-		Leu	Ala	Ile	Val		Asp	Ser	Pro	Gln	555 Asp	Ser	ጥህም	Gln	T.e.ı	560
					565		۲			570	rap	.uel	TYL	LILL	575	ny s
	Ile	Arg	Val	Arg 580	His	Asn	Àsn	Lys	Leu 585		Arg	Glu	Lys	Tyr 590		Glu
55	His	Glu	Ile		Leu	Glu	Val	Tyr		Cys	Arg	Lys	Ser	His	Asp	His

			595					600					605			
	Asn	Glu	Pro	Ile	Ile	Leu	Ser	Gln	Gln	Ser	Thr	Gly	Phe	Gln	Trp	Ala
		610					615					620				
_	Phe	Asn	Phe	Met	Phe	Gly	Phe	Leu	Tyr	Asn	Val	Gly	Ser	His	Phe	Ser
5 -	625					630					635					640
	Phe	Asn	His	Asn		Ile	Tyr	Val	Met		Glu	Pro	Ala	Thr	His	Leu
		· ·			645					650					655	
	Ser	Val	Pro		Arg	Lys	Glu	Phe		Lys	Phe	Leu	Lys		Tyr	Ala
10	*** -	T	<b>3</b>	660	17-7	ml	n	**- 1	665		m1	••••	<b>-</b>	670	_,	_
10	HIS	гуя	675	HIS	vaı	THE	Pne	680	Leu	Ala	Thr	HIS	_	Pro	Phe	Leu
	Val	λen		Aen	Hie	Len	Agn		Tla	A ro	Tla	17 a 1	685	Lve	Glu	Thr
	var	690	1311	Map	1113	пец	695	GIU	TTE	Arg	116	700	GIU	пуз	Gru	THE
	Glu		Ser	Val	Ile	Lvs		His	Phe	Asn	Tvr		Len	Asn	Asn	Δla
15	705	4				710					715					720
	Ser	Lys	Asp	Ser	Asp	Ala	Leu	Asp	Lys	Ile	Lys	Arg	Ser	Leu	Gly	Val
					725				-	730	-	_			735	
	Gly	Gln	His	·Val	Phe	His	Asn	Pro	Gln	Lys	His	Arg	Ile	Ile	Phe	Val-
••				740					745					750		
20	Glu	Gly		Thr	Asp	Tyr	Cys		Leu	Ser	Ala	Phe		Leu	Tyr	Leu
•	•	m	755	<b>a</b> 3	<b></b>	<b>T</b>	<b>3</b>	760	_				765		_	_
	arg	770	гÀг	GIU	ıyr	Lys	775	Asn	Pro	TIE	Pro		Thr	Phe	Leu	Pro
	Tle		GI v	T. <del>e</del> 11	Lve	Δen	-	Sar	Acn	λan	Mot	780	Gl 11	Thr	Ile	Glu.
25	785	Ser	GLY	Leu	шуз	790	лър	361	Mali	Азр	795	ьуѕ	GIU	1111	116	800
		Leu	Cvs	Glu	Leu		Asn	His	Pro	Ile		Lėu	Thr	Asp	Asp	
•	•		•		805	. •				810					815	
	Arg	Lys	Cys	Val	Phe	Asn	Gln	Gln	Ala	Thr	Ser	Glu	Arg	Phe	Lys	Arg
				820					825					830		
30	Ala	Asn		Glu	Met	His	Asp		Ile	Thr	Ile	Leu	Gln	Leu	Ser	Asp
		_	835	•		_		840					845			
-	Cys		Arg	His	Phe	Lys		Ile	Glu	Asp	Cys		Ser	Ala	Asn	Asp
	7	850	, T	TT	n1-	T	855	*	<b>~1</b> ~		01	860				Dh.
35	865	ASII	ьys	LYE	AId	LуS 870	ASII	ьys	GIN	Met	875	Leu	Ser	Mec	Ala	880
33		Thr	Ara	Len	Leu		Glv	Glv	Glu	Aen		Tla	Glu	Laze	Gln	
	-1-		5		885	-1-				890	7114		014	275	895	
	Lys	Arg	Asn	Phe		Lys	Leu	Phe	Lys	_	Ile	Ala	Trp	Ala	Thr	Asn
		•		900		-			905	•			•	910		
40	Leu	Ile	Lys	Asn												
			915													

### (2) INFORMATION FOR SEQ ID NO:98:

- 45 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 176 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 50 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
- 55 (A) ORGANISM: Helicobacter pylori

```
(ix) FEATURE:
                (A) NAME/KEY: misc_feature
                (B) LOCATION 1...176
  5
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:
     Met Thr Ala Met Met Arg Tyr Phe His Ile Tyr Ala Thr Thr Phe Phe
                                          10
 10
     Phe Pro Leu Ala Leu Leu Phe Ala Val Ser Gly Leu Ser Leu Leu Phe
     Lys Ala Arg Gln Asp Thr Gly Ala Lys Ile Lys Glu Trp Val Leu Glu
     Lys Ser Leu Lys Lys Glu Glu Arg Leu Asp Phe Leu Lys Gly Phe Ile
15
     Lys Glu Asn His Ile Ala Met Pro Lys Lys Ile Glu Pro Arg Glu Tyr
     Arg Gly Ala Leu Val Ile Gly Thr Pro Leu Tyr Glu Ile Asn Leu Glu
     Thr Lys Gly Thr Gln Thr Lys Ile Lys Thr Ile Glu Arg Gly Phe Leu
     Gly Ala Leu Ile Met Leu His Lys Ala Lys Val Gly Ile Val Phe Gln
                                 120
     Ala Leu Leu Gly Ile Phe Cys Val Phe Leu Leu Leu Phe Tyr Leu Ser
                          135
                                                 140
     Ala Phe Leu Met Val Ala Phe Lys Asp Thr Lys Arg Met Phe Ile Ser
                         150
                                             155
     Val Leu Ile Gly Ser Val Val Phe Phe Gly Ala Ile Tyr Trp Ser Leu
                                         170
30
     (2) INFORMATION FOR SEQ ID NO:99:
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 222 amino acids
35
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
40
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...222
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:
50
    Met Phe Lys Asn Ala Leu Asn Ile Gln Asp Phe Ser Phe Lys Asn His
     Thr Ser Thr Ala Ile Ile Gly Thr Asn Gly Ala Gly Lys Ser Thr Leu
55
     Ile Asn Thr Ile Leu Gly Ile Arg Ser Asp Tyr Asn Phe Lys Ala Gln
```

- 173 - -

			35					40					45			
	Asn	Asn	Asn	Ile	Pro	Tyr	His	Asp	Asn	Val	Ile	Pro	Gln	Arg	Lys	Gln
		50					55					60				
	Leu	Gly	Val	Val	Ser	Asn	Leu	Phe	Asn	Tyr	Pro	Pro	Gly	Leu	Asn	Ala
5	65				•	70					75					80
	Asn	Asp	Leu	Phe	Lys	Phe	Tyr	Gln	Phe	Phe	His	Lys	Asn	Cys	Thr	Leu
					85					90					95	
	Asp	Leu	Phe	Glu	Lys	Asn	Leu	Leu		_		Tyr	Glu		Leu	Ser
••	:	_	·	100		_	_	_	105					110		
10				Lys					Ile	Asp	Leu	Ala		Ser	His	His
				77-7				120	<b>D</b>		m1		125	~1		•
	Pro		Leu	Val	TTE			GIU	Pro	GIU	Tnr		ьeu	GIU	GIN	Asn
	7.7	130	71.0	Arg	T on	Cor		T 033	T1.0	Com	7	140	7.00	mb	<b>~1</b> -	<b>71</b> m
15	145	neu	116	Arg	neu	150	ASII	Leu	TIE	ser	155	Arg	Waii	1111	GIII	160
13		Thr	Ser	Ile	Tle		Thr	Hig	Asn	Pro		Va l	. T.e.n	Agn	Sar	
	DCu	1111	DCI.		165			******	r.op	170	110		2504		175	
	Glu	Tro	Val	Leu		Leu	Lvs	Asn	Glv		Ile	Ala	Gln			
				180					185					190	-2-	
20	Leu	Asn	Ser	Ile	Leu	Lys	Ser	Val	Ala	Lys	Thr	Phe	Asn	Phe	Lys	Glu
			195			,		200					205		-	
	Lys	Pro	Thr	Thr	Lys	Asp	Leu	Leu	Ala	Leu	Leu	Lys	Asp	Ile		•
		210					215					220				
25	(2)	INF	ORMA'	rion	FOR	SEQ	ID I	NO:10	00:							
		(i)		QUEN												
				A) LI					acı	as						
30			-	B) T D) T(												
50			(1	)) 10	)POT	JG1 :	T T116	Eal								
		(ii)	MOI	LECU	LE T	YPE:	prof	tein								
		,,					<b>P</b> -0.								•	
		(i <b>i</b> i)	HYI	POTH	ETIC	AL: 3	YES									
35																
		(vi)	OR:	IGIN	AL S	OURC	Ε:				•					
			(2	A) OI	RGAN	ISM:	Hel:	icoba	acte	r py:	lori					
40		(ix)		ATURI				_								
40				A) N2						е		•				
			(1	B) LO	OCAT:	ION :	14	406								
		(		```	7D D1	acan.	TDMT/	ONT		N						
:		(XI)	SEG	OUEN(	וע פי	SSCR.	IPTIC	JN: 3	SEQ.	TD M	):10	):				
45	Met	Тче	Δla	Ala	Hig	Pro	Tle	Targ	Dro	Tla	Lve	Δla	Dro	Larg	T.e.11	T.ve
٠,	1	- 7 -	AIU	7114	5	110	-,	Lys	110	10	Dys	AIG	110	Буз	15	275
		Gln	Phe	Leu	-	Aro	Val	Phe	Va1		Ala	Ser	Ile.	Āro		Tro
				20	9				25	1				30	5	P
	Asn	Asp	Gln	Ala	Cvs	Pro	Leu	Glu		Val	Glu	Leu	Asp		Gln	Ala
50			35		4			40					45	_1_		
	His	Lys	Ala	Met	Ile	Ala	Tyr	Leu	Leu	Ala	Lys	Asp	Leu	Lys	Asp	Arg
		50					55				-	60		•	-	
	Gly	Lys	Asp	Leu	Asp	Leu	Asp	Leu	Leu	Ile	Lys	Tyr	Phe	Cys	Phe	Glu
	65				,	70					75					80
66			~ 1				T	mat.	_	- 3	-	_	-		-1	-

					85		•			90					95	
•	Ala	Leu	Gln	Gln 100	Thr	His	Ser	Lys	Glu 105		Ala	Ser	Tyr			Gln
	Ser	Leu	Gln			Ile	Ser	Δla			Sar	Lan	Cl.	110	T 011	Lys
5			115					120					125			
	Glu	Tyr 130	Leu	Ser	His	Arg	Pro 135	Gln	Ile	Leu	Glu			Ile	Leu	Glu
	Ser			Dhe	Tran	. או			(T)	<b>~</b> 3		140			_	
	145	mu	1115	1116	+ y -	150	261	гåз	пр	GIU	155	Asp	TIE	Ile	тут	His 160
10	Phe	Asn	Pro	Asn	Met 165	Tyr		Val	Lys	Glu 170		Lys	Asp	Lys		Asp
	Lys	Gln	Leu	His					Leu			Glv	Leu	Phe	175 Glv	Glu
				180					185					190		
15			195					200					205			Phe
	Gln	Lys	Arg	Trp	Ser	Gln	Thr	Pro	Arg	Val	Pro	Gln	Thr	Ser	Val	Leu
		210		T		17- 1	215					220				
	225	птѕ	Int	Leu	Cys	Val 230	Ala	IIe	Met	Gly	Tyr 235	Leu	Leu	Ser	Phe	Asp 240
20	Leu	Lys	Ala	Cys	Lys	Ser	Met	Arq	Ile	Asn		Phe	Len	Glv	Glv	Leu
					245					250					255	
				260		Glu			265					270		
25	Lys	Gln	Ser	Val	Ala	Gly	Leu	Asp	His	Cys	Ile		Glu	Ile	Glu	Lys
23	T		275	<b>03</b> -	3	<b>T</b>		280					285			
		290				Lys	295	•				300				
	Glu	Asp	Leu	Lys	Tyr	Phe	Thr	Glu	Asn	$\operatorname{Glu}$	Phe	Lys	Asn	Arg	Tyr	Lys
20	305					310					315					320
30 .	Asp	Lys	Ser	His	Gln 325	Ile	Val	Phe	Thr	Lys	Asp	Ala		Glu		Phe
	Thr	Leu	Tvr	Asn		Asp	Glu	ጥህጕ	T.em		. 37-1	~	01	G1	335	•
				340					345					350		
35	Lys	Val	Cys	Asp	His	Leu			Phe	Leu	Glu	Ala	Gln	Ile	Ser	Leu
33	Sor.		355	T1.				360	_			_	365			
	ser	370	GTA	TTE	ser	Ser	1yr	Asp	Leu	Ile	Gln		Ala	Lys	Asn	Leu
	Leu		Leu	Ara		Gln		Glu	T.e.11	T.Ou	λen	380	7 ~~	Ton	<b>01</b>	T
	385					390		<b>724</b>		ے۔ د	395		vab	neu	GIA	ьуs 400
40	Leu	Phe	Arg	Asp	Phe		•				,,,,	•	•			400
					405	_										
	(2)	INFO	RMAT	NOI	FOR	SEQ	ID N	ю:10	1:				1		-	:
45	•	(1)	SEC	TENC	ידי ריב	מממנה	י מיםיוי	COTA								

45 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 335 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- 50 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE:

  (A) ORGANISM: Helicobacter pylori

WO 98/18323 PCT/US97/19575

- 175 -

### (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...335

5

### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

			,,	·													
	*	Val	Leu	Trp	Val	Leu	Tyr	Phe	Leu	Thr	Ser	Leu	Phe	Ile	Cys	Ser	Leu
		1		_		5	-				10				-	15	
1	0	Ile	Val	Leu	$\mathtt{Trp}$	Ser	Lys	Lys	Ser	Met	Leu	Phe	·Val	Asp	Asn	Ala	Asn
					20					25					30		
		Lys	Ile		Gly	Phe	His			Arg	Thr	Pro	Arg		Gly	Gly	Leu
				35	_		_,		40				_	45	_	-1	
1	5	Gly		Phe	Leu	Ser	Phe	AIA 55	Leu	Ala	Cys	Tyr		Glu	Pro	Phe	Glu
ı	)	Mot	50 Bro	Dha	Luc	Glv	Dro		Va I	Dhe	Lou	G1 v	60 Tev	Ser	Len	Va I	Pho
		65	FIU	FILE	<b>- - - - - - - - - -</b>	,019	70	1110	Val	FIIC	iie u	75	Den	Der	neu	VAI	80
			Ser	Gly	Phe	Leu	Glu	Asp	Ile	Asn	Leu	Ser	Leu	Ser	Pro	Lys	
				-		85		-			90					95	
2	.0	Arg	Leu	Ile	Leu	Gln	Ala	Val	Gly	Val	Val	Cys	Ile	Ile	Ser	Ser	Thr
					100					105					110		
		Pro	Leu		Val	Ser	Asp	Phe		Pro	Leu	Phe	Ser	Leu	Pro	Tyr	Phe
		<b>7</b> 1 -		115	T	Dha	77-	T1'-	120	<b>W</b> = 4	T	**- 1	<b>61</b>	125	0	3	*1-
2	.5	TIE	130	Pne	Leu	Pne	ALA	135	Pne	met	Leu	vai	140	Ile	ser	ASN	АТА
_	,,,	Ile		Ile	Ile	Asp	Glv		Asn	Glv	Leu	Ala		Gly	Ile	Cvs	Ala
		145					150			,		155.		7		-2,-	160
		Ile	Ala	Leu	Leu	Val	Ile	His	Tyr	Ile	Asp	Pro	Ser	Ser	Leu	Ser	Cys
			•		-	165					170	-				175	
-3	0 -	Leu	Leu	Ala		Met	Val.	Leu	Gly		Met	Val	Leu	Asn		Pro	Ser
				-1-	180	•	<b>53</b>	•	~1	185		_	_,	_	190		••••
		GIY	ьуs		Pne	Leu	GIY	Asp	200	GIY	Ата	Tyr	Pne	Leu	GTA	Leu	vaı
		Cya.	Glv	195 Tle	Ser	T.e11	T.e.ii	Hiq		Ser	T.em	Glu	Gln	205 Lys	Tle	Ser	Val
3	5	Cyb	210					215			204		220	<b>D</b> , <b>S</b>			
		Phe	Phe	Gly	Leu	Asn	Leu	Met	Leu	Tyr	Pro	Val	Ile	Glu	Val	Leu	Phe
		225	•	_			230			-		235					240
		Ser	Ile	Leu	Arg	Arg	Lys	Ile	Lys	Arg		Lys	Ala	Thr	Met	Pro	Asp
	^	_		1	_	245		_	_ :		250		_			255	_
4	0	Asn	Leu		Leu 260	His	Thr	Leu	Leu	265	rys	Phe	Leu	Gln	G1n 270	Arg	Ser
		Dhe	Δen			Δαη	Pro	Len	Cvs		Dhe	Tla	T.em	Ile		Cvs	Δen
		FIIC	Apii	275	110	no	110	Deu	280	AIG	rne	116	Deu	285	Пеп	Cys	no
		Leu	Pro	Phe	Ile	Leu	Ile	Ser	Val	Leu	Phe	Arg	Leu	Asp	Ala	Tyr.	Ala
4	5		290					295				_	300	-		-	
		Leu	Ile	Val	Ile	Ser	Leu	Val	Phe	Ile	Ala	Cys	Tyr	Leu	Ile	Gly	Tyr
		305					310					315					320
		Ala	Tyr	Leu	Asn	-	Gln	Val	Cys	Ala		Glu	Lys	Arg	Ala		
-	0					325					330					335	
J	v																

(2) INFORMATION FOR SEQ ID NO:102:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 96 amino acids
- 55 (B) TYPE: amino acid

(D	) TO	COTO	GΥ	: /1	ine	ear
----	------	------	----	------	-----	-----

- (ii) MOLECULE TYPE: protein
- 5 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

- 10 (ix) FEATURE:
  - (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...96
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

Met Lys Lys Val Ile Val Ala Leu Gly Val Leu Ala Phe Ala Asn Val

Leu Met Ala Thr Asp Val Lys Ala Leu Val Lys Gly Cys Ala Ala Cys

20 His Gly Val Lys Phe Glu Lys Lys Ala Leu Gly Lys Ser Lys Ile Val
35 40 45

Asn Met Met Ser Glu Lys Glu Ile Glu Glu Asp Leu Met Ala Phe Lys 50 55 60

- Ser Gly Ala Asn Lys Asn Pro Val Met Thr Ala Gln Ala Lys Lys Leu 75 75 80 80 Ser Asp Glu Asp Ile Lys Ala Leu Ala Lys Tyr Ile Pro Thr Leu Lys 85 90
- (2) INFORMATION FOR SEQ ID NO:103:

30

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 156 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

35

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: YES
- 40 (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc\_feature
- 45 (B) LOCATION 1...156
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

Asn Ala Val Phe Glu Lys Leu Asp Leu Glu Phe Lys Asp Gly Leu Ser

Ala Ile Ser Gly Ala Ser Gly Val Gly Lys Ser Val Leu Ile Ala Ser

55 Leu Leu Gly Ala Phe Gly Leu Lys Glu Ser Asn Ala Ser Asn Ile Glu

Val Glu Leu Ile Ala Pro Phe Leu Asp Thr Glu Glu Tyr Gly Ile Phe 70 Arg Glu Asp Glu His Glu Pro Leu Val Ile Ser Val Ile Lys Lys Glu 90 Lys Thr Arg Tyr Phe Leu Asn Gln Thr Ser Leu Ser Lys Asn Thr Leu 100 105 Lys Ala Leu Leu Lys Gly Leu Ile Lys Arg Leu Ser Asn Asp Arg Phe 120 125 Ser Gln Asn Glu Leu Asn Asp Ile Leu Met Leu Ser Leu Leu Asp Gly 135 140 Tyr Ile Gln Asn Lys Asn Arg Arg Leu Ala Pro Phe 15 (2) INFORMATION FOR SEQ ID NO:104: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 118 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: 30 (A) NAME/KEY: misc feature (B) LOCATION 1...118 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104: Val Met Leu Met Ala Ile Phe Thr Pro Tyr Ile Leu Ile Leu Lys Met Met Lys Lys Ser Met Ser Leu Phe Ala Asn Met Gly Leu Glu Gln Ile Phe Cys Asn Arg Asp Ile Lys Asp Leu Asn Asp Phe Val Phe Gly Ile 40 Glu Val Gly Leu Asp Ser Asn Ala Arg Lys Asn Arg Ser Arg Lys Ala 55 Met Glu Asn His Leu Ile Gly Leu Phe Val Gln Ala Gln Leu Asn Phe 70 75 Lys Glu Gln Val Asp Ile Arg Glu Phe Glu Asp Leu Arg Gln Ala Phe 90 Gly Asn Asp Thr Lys Lys Phe Asp Phe Val Ile Phe Ser Lys Glu Lys 100 105 Thr Tyr Phe His Arg Ser 50 115 (2) INFORMATION FOR SEQ ID NO:105: (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 355 amino acids

```
(B) TYPE: amino acid(D) TOPOLOGY: linear
```

(ii) MOLECULE TYPE: protein

5

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

10

(ix) FEATURE:

(A) NAME/KEY: misc\_feature

(B) LOCATION 1...355

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Met Asn Ile Lys Ile Leu Lys Ile Leu Val Gly Gly Leu Phe Phe Leu Ser Leu Asn Ala His Leu Trp Gly Lys Gln Asp Asn Ser Phe Leu Gly 20 Ile Gly Glu Arg Ala Tyr Lys Ser Gly Asn Tyr Ser Lys Ala Ala Ser 40 Tyr Phe Lys Lys Ala Cys Asn Asp Gly Val Ser Glu Gly Cys Thr Gln 55 25 Leu Gly Ile Ile Tyr Glu Asn Gly Gln Gly Thr Arg Ile Asp Tyr Lys Lys Ala Leu Glu Tyr Tyr Lys Thr Ala Cys Gln Ala Asp Asp Arg Glu 85 90 Gly Cys Phe Gly Leu Gly Gly Leu Tyr Asp Glu Gly Leu Gly Thr Ala 30 100 Gln Asn Tyr Gln Glu Ala Ile Asp Ala Tyr Ala Lys Ala Cys Val Leu 120 Lys His Pro Glu Ser Cys Tyr Asn Leu Gly Ile Ile Tyr Asp Arg Lys 135 Ile Lys Gly Asn Ala Ala Gln Ala Val Thr Tyr Tyr Gln Lys Ser Cys Asn Phe Asp Met Ala Lys Gly Cys Tyr Ile Leu Gly Thr Ala Tyr Glu 170 Lys Gly Phe Leu Glu Val Lys Gln Ser Asn His Lys Ala Val Ile Tyr 40 Tyr Leu Lys Ala Cys Arg Leu Asn Glu Gly Gln Ala Cys Arg Ala Leu 200 Gly Ser Leu Phe Glu Asn Gly Asp Ala Gly Leu Asp Glu Asp Phe Glu 215 220 Val Ala Phe Asp Tyr Leu Gln Lys Ala Cys Ala Leu Asn Asn Ser Gly 45 235 Gly Cys Ala Ser Leu Gly Ser Met Tyr Met Leu Gly Arg Tyr Val Lys Lys Asp Pro Gln Lys Ala Phe Asn Tyr Phe Lys Gln Ala Cys Asp Met 50 265 Gly Ser Ala Val Ser Cys Ser Arg Met Gly Phe Met Tyr Ser Gln Gly 280 Asp Thr Val Ser Lys Asp Leu Arg Lys Ala Leu Asp Asn Tyr Glu Arg 295 Gly Cys Asp Met Gly Asp Glu Val Gly Cys Phe Ala Leu Ala Gly Met

WO 98/18323 PCT/US97/19575

- 179 -

310 Tyr Tyr Asn Met Lys Asp Lys Glu Asn Ala Ile Met Ile Tyr Asp Lys 330 325 Gly Cys Lys Leu Gly Met Lys Gln Ala Cys Glu Asn Leu Thr Lys Leu Arg Gly Tyr 355 (2) INFORMATION FOR SEQ ID NO:106: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 193 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear 15 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: (A) NAME/KEY: misc feature 25 (B) LOCATION 1...193 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106: Met Lys Glu Lys Asn Phe Trp Pro Leu Gly Ile Met Ser Val Leu Ile 30 10 Phe Gly Leu Gly Ile Val Val Phe Leu Val Val Phe Ala Leu Lys Asn Ser Pro Lys Asn Asp Leu Val Tyr Phe Lys Gly His Asn Glu Val Asp 40 Leu Asn Phe Asn Ala Met Leu Lys Thr Tyr Glu Asn Phe Lys Ser Asn Tyr Arg Phe Ser Val Gly Leu Lys Pro Leu Thr Glu Ser Pro Lys Thr 70 75 Pro Ile Leu Pro Tyr Phe Ser Lys Gly Thr His Gly Asp Lys Lys Ile 40 85 90 Gln Glu Asn Leu Leu Asn Asn Ala Leu Ile Leu Glu Lys Ser Asn Thr 105 Leu Tyr Ala Gln Leu Gln Pro Leu Lys Pro Ala Leu Asp Ser Pro Asn 120 45 Ile Gln Val Tyr Leu Ala Phe Tyr Pro Ser Gln Ser Gln Pro Arg Leu 135 140 Leu Gly Thr Leu Asp Cys Lys Asn Ala Cys Glu Pro Leu Lys Phe Asp 150 155 Leu Leu Glu Gly Asp Lys Val Gly Arg Tyr Lys Ile Leu Phe Lys Phe 50 165 \_ 170 Val Phe Lys Asn Lys Glu Glu Leu Ile Leu Glu Gln Leu Ala Phe Phe 180 185

Lys

```
(2) INFORMATION FOR SEQ ID NO:107:
```

```
(i) SEQUENCE CHARACTERISTICS:
```

- (A) LENGTH: 289 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- 10 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

- 15 (ix) FEATURE:
  - (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...289
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

Leu Gly Ile Asn Met Cys Ser Lys Lys Ile Arg Asn Leu Ile Leu Cys

1 5 10 15

Phe Gly Phe Ile Leu Ser Leu Cys Ala Glu Glu Asn Ile Thr Lys Glu
20 25 30

25 Asn Met Thr Glu Thr Asn Thr Thr Glu Glu Asn Thr Pro Lys Asp Ala
35 40

Pro Ile Leu Leu Glu Glu Lys Arg Ala Gln Thr Leu Glu Leu Lys Glu
50 55 60

Glu Asn Glu Val Ala Lys Lys Ile Asp Glu Lys Ser Leu Leu Glu Glu 30 65

65 70 75 80 Ile His Lys Lys Lys Arg Gln Leu Tyr Met Leu Lys Gly Glu Leu His

85 90 95
Glu Lys Asn Glu Ser Ile Leu Phe Gln Gln Met Ala Lys Asn Lys Ser

100 105 110

Gly Phe Phe Ile Gly Val Ile Leu Gly Asp Ile Gly Ile Asn Ala Asn 115 120 125

Pro Tyr Glu Lys Phe Glu Leu Leu Ser Asn Ile Gln Ala Ser Pro Leu 130 135 140

Leu Tyr Gly Leu Arg Ser Gly Tyr Gln Lys Tyr Phe Ala Asn Gly Ile
40 145 150 155

Ser Ala Leu Arg Phe Tyr Gly Glu Tyr Leu Gly Gly Ala Met Lys Gly
165 170 175

Phe Lys Ser Asp Ser Leu Ala Ser Tyr Gln Thr Ala Ser Leu Asn Ile 180 185 190

45 Asp Leu Leu Met Asp Lys Pro Ile Asp Lys Glu Lys Arg Phe Ala Leu
195 200 205

Gly Ile Phe Gly Gly Val Gly Val Gly Trp Asn Gly Met Tyr Gln Asn 210 215 220

Leu Lys Glu Ile Arg Gly Tyr Ser Gln Pro Asn Ala Phe Gly Leu Val 225 230 235 240

Leu Asn Leu Gly Val Ser Met Thr Leu Asn Leu Lys His Arg Phe Glu
245 250 255

Leu Ala Leu Lys Met Pro Pro Leu Lys Glu Thr Ser Gln Thr Phe Leu 260 265 270

55 Tyr Tyr Phe Lys Ser Thr Asn Ile Tyr Tyr Ile Ser Tyr Asn Tyr Leu

- 181 -

275 280 285 Leu 5 (2) INFORMATION FOR SEQ ID NO:108: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 668 amino acids (B) TYPE: amino acid 10 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 15 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: 20 (A) NAME/KEY: misc\_feature (B) LOCATION 1...668 (xi) SEQUENCE DESCRIPTION: SEO ID NO:108: Met Arg Lys Leu Phe Ile Pro Leu Leu Phe Ser Ala Leu Glu Ala 10 Asn Glu Lys Asn Gly Phe Phe Ile Glu Ala Gly Phe Glu Thr Gly Leu 25 Leu Glu Gly Thr Gln Thr Gln Glu Lys Arg His Thr Thr Lys Asn 30 40 Thr Tyr Ala Thr Tyr Asn Tyr Leu Pro Thr Asp Thr Ile Leu Lys Arg Ala Ala Asn Leu Phe Thr Asn Ala Glu Ala Ile Ser Lys Leu Lys Phe Ser Ser Leu Ser Pro Val Arg Val Leu Tyr Met Tyr Asn Gly Gln Leu 90 Thr Ile Glu Asn Phe Leu Pro Tyr Asn Leu Asn Asn Val Lys Leu Ser 105 Phe Thr Asp Ala Gln Gly Asn Thr Ile Asp Leu Gly Val Ile Glu Thr 40 120 Ile Pro Lys His Ser Lys Ile Val Leu Pro Gly Glu Ala Phe Asp Ser 135 Leu Lys Glu Ala Phe Asp Lys Ile Asp Pro Tyr Thr Leu Phe Leu Pro 150 155 45 Lys Phe Glu Ala Thr Ser Thr Ser Ile Ser Asp Thr Asn Thr Gln Arg 165 Val Phe Glu Thr Leu Asn Asn Ile Lys Thr Asn Leu Ile Met Lys Tyr 185 Ser Asn Glu Asn Pro Asn Asn Phe Asn Thr Cys Pro Tyr Asn Asn Asn 50 200

Gly Asn Thr Lys Asn Asp Cys Trp Gln Asn Phe Thr Pro Gln Thr Ala

Glu Glu Phe Thr Asn Leu Met Leu Asn Met Ile Ala Val Leu Asp Ser

Gln Ser Trp Gly Asp Ala Ile Leu Asn Ala Pro Phe Glu Phe Thr Asn

220

235

215

									•							
					245	5				250	`		٠.		255	. ,
	Ser	Sei	r Thi	Asr			Ser	^ Asr	Dro	25t	J C. Tarr		. 3703	1 7	255	Gly
				260	) 1				265		. цу	, cys	va.	270		GIY
	Va]	. Asr	ı Gly	/ Arg	y Val	. Asr	Thr	Lys			Glr	ı Glr	ነ	r Tle	, . T.e.:	Asn
5			275	•				280	)				285	5		
	Lys	Glr	ı Gly	/ Ile	: Ile	: Asr	Asr	Phe	Arg	Lys	Lys	Ile	Glu	1 Ile	. Asp	Ala
		290	,				295	5				300	ł .			
	Val	. Val	Leu	ı Lys	Asn	Ser	Gly	/ Val	.Val	Gly	Leu	ı Ala	Asr	ı Gly	Tyr	Gly
10	303	,				310	,				315	i				320
10	Asn	. Asp	GT?	GIU	Tyr	Gly	Thr	Leu	Gly			Ala	Tyr	Ala	Leu	Asp
	Dre	Larc	· T.,		325			_	_	330	)				335	
	110	. Lya	УLLYS	340	PHE	: Сту	ASI	l Asp	Leu	Lys	Thr	Ile	Asn		Glu	Asp
	Leu	Arc	Thr			Hie	Gl <sub>11</sub>	Dho	345		mi			350		
15			355				, GIU	360	ser	HIS	Inr	. rās			Gly	His
	Asn	Gly	/ Asn	Met	Thr	Tyr	Gln	Ara	Val	Pro	1757	Thr	365	) Name	Gly	<b>~1</b>
		3/0	,				375					380				
	Val	Glu	Lys	Asp	Ser	Asn	Gly	Lys	Pro	Lys	Asp	Ser	Asp	Glv	Leu	Pro
20	202					390					305					400
20	Tyr	Asn	. Val	Cys	Ser	Leu	Tyr	Gly	Gly	Ser	Asn	Gln	Pro	Ala	Phe	Pro
					405					410					415	
	ser	ASI	Tyr	Pro	Asn	Ser	Ile	Tyr	His	Asn	Cys	Ala	Asp	Val	Pro	Ala
	Glv	Phe	T.A.	420		The	77-	27-	425	_		_		430		
25	- J		435	GLY	vai	ŤIII	Ara	440	val	Trp	Gln	Gln			Asn	Gln
	Asn	Ala			Ile	Asn	Tvr		Δen	T.611	C3	C	445	Mb	Asn	_
		450					455		77011	neri	GIY	460	GIU	Inr	Asn	Tyr
	Asn	Leu	Asn	Ala	Ser	Leu	Asn	Thr	Gln	Asp	Leu	Ala	Asn	Ser	Met	T.e.11
20	400					470					475					480
30	Ser	Thr	Ile	Gln	Lys	Thr	Phe	Val	Thr	Ser	Ser	Val	Thr	Asn	His	His
					485					490					495	
	Pne	ser	Asn	Ala	Ser	Gln	Ser	Phe		Ser	Pro	Ile	Leu	Gly	Val	Asn
	Δla	Lve	Tla	500	The seas	<b>~1</b>		_	505	_				510		
35	n.u	Lys	515	GIY	Tyr	GIN	ASD	Tyr	Phe	Asn	Asp	Phe		Gly	Leu	Ala
	Tyr	Tvr		Ile	Tle	Lvs	Tyr	520	Тъ съ	71-			525		Gln	_
	•	530	1			-75	535	ASII	TÄT	AIA	Lys	A1a 540	vaı	Asn	GIn	Lys
	Val	Gln	Gln	Leu	Ser	Tyr	Gly	Glv	Glv	Ile	Asp	J-211	T.em	T.011	Asp	Dho
40	247					.55U				-	555					560
40	Ile	Thr	Thr	Tyr	Ser	Asn	Lys	Asn	Ser	Pro	Thr	Gly	Ile	Gln	Thr	Lvs
					565					570					575	
	Arg	Asn	Phe	Ser	Ser	Ser	Phe	Gly	Ile	Phe	Gly	Gly	Leu	Arg	Gly	Leu
,				280		•			585					590		
45	TYL	WOII	595	Tyr	Tyr	vaı	Leu	Asn	Lys	Val	Lys	Gly	Ser	Gly	Asn	Leu
	Asp	Val		Thr	Glv	T.011	Λαπ	600	3	m	_		605			
		610		****	Gry	neu.	615	ıyr	Arg	Tyr	Lys		Ser	Lys	Tyr	Ser
	Val		Ile	Ser	Ile	Pro		Tle	Gln	λ~~	T	620	O	77- T	Val	_
	625	•				630			GTIİ	ar g	635	wrg	ser	vai		
50	Ser	Gly	Gly	Asp	Tyr		Asn	Ser	Phe	۷a٦	Phe	Asn	G] 11	G) v	Ala	640 Ser
					045					650			J_ U	O.L.Y	655	∩ <i>⊏</i> 1
	His.	Phe	Lys	Val	Phe	Phe	Asn	Tyr	Gly	Trp	Val	Phe				
				660		٠			665			-				
FF																

55 (2) INFORMATION FOR SEQ ID NO:109:

	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 63 amino acids
	(B) TYPE: amino acid
5	(D) TOPOLOGY: linear
_	(b) Totoboot. Ifficat
	(ii) MOLECULE TYPE: protein
	122, 110
	(iii) HYPOTHETICAL: YES
10	
	(vi) ORIGINAL SOURCE:
	(A) ORGANISM: Helicobacter pylori
	F,2000
	(ix) FEATURE:
15	(A) NAME/KEY: misc feature
•	(B) LOCATION 163
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:
	·
20	Met Asn Thr Glu Ile Leu Thr Ile Met Leu Val Val Ser Val Leu Met
	1 5 10 15
	Gly Leu Val Gly Leu Ile Ala Phe Leu Trp Gly Val Lys Ser Gly Gli
	20 25 30
25	Phe Asp Asp Glu Lys Arg Met Leu Glu Ser Val Leu Tyr Asp Ser Ala
25	35 40 45
	Ser Asp Leu Asn Glu Ala Ile Leu Gln Glu Lys Arg Gln Lys Asn
	50 55 60
	(2) THEODMARTON HOD GEO TO NO 410
30	(2) INFORMATION FOR SEQ ID NO:110:
30	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 406 amino acids
	(B) TYPE: amino acid
	(D) TOPOLOGY: linear
35	(0, 00000000000000000000000000000000000
	(ii) MOLECULE TYPE: protein
	(iii) HYPOTHETICAL: YES
40	(vi) ORIGINAL SOURCE:
	(A) ORGANISM: Helicobacter pylori
	(ix) FEATURE:
	(A) NAME/KEY: misc_feature
45	(B) LOCATION 1406
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:
<b></b>	Met Val Phe Phe His Lys Lys Ile Ile Leu Asn Phe Ile Tyr Ser Leu
50	1 5 10 15
	Met Val Ala Phe Leu Phe His Leu Ser Tyr Gly Val Leu Leu Lys Ala
	20 25 30
	Asp Gly Met Ala Lys Lys Gln Thr Leu Leu Val Gly Glu Arg Leu Val
55	35 40 45
55	Trp Asp Lys Leu Thr Leu Leu Gly Phe Leu Glu Lys Asn His Ile Pro

		50					55					60					
	Gln	Lys	Leu	Tyr	Tyr	Asn	Leu	Ser	Ser	Gln	Asp	Lys	Glu	Leu	Ser	Ala	
	65					70					75					80	
	Glu	Ile	Gln	Ser	Asn	Val	Thr	Tyr	Tyr	Thr	Leu	Arg	Asp	Ala	Asn	Asn	
5					85					90					95		
	Thr	Leu	Ile	Gln	Ala	Leu	Ile	Pro	Ile	Ser	Gln	Asp	Leu	Gln	Ile	His	
				100					105					110			
	Ile	Tyr	Lys	Lys	Gly	Glu	Asp	Tyr	Phe	Leu	Asp	Phe	Ile	Pro	Ile	Val	
10			115					120					125				
10	Phe	Thr	Arg	Lys	Glu	Arg	Thr	Leu	Leu	Leu	Ser	Leu	Gln	Thr	Ser	Pro	
		130					135				•	140					
	Tyr	GIn	Asp	ITe	Val	Lys	Ala	Thr	Asn	Asp	Pro	Leu	Leu	Ala	Asn	Gln	
	145				_	150					155					160	
15	ьeu	Met	ASI	Ата	Tyr	Lys	Lys	Ser	Val			Lys	Arg	Leu	Val	Lys	
13	3.00	7	T	<b>-</b> 1-	165				_	170					175		
	ASII	Asp	гÀг	TTE	Ala	Ile	Val	Tyr	Thr	Arg	Asp	Tyr	Arg	Val	Gly	Gln	
	פומ	Dhe	GI v	180		mia	71.		185					190			
	ALU	FIIC	195	GIII	FIO	Thr	тте	ьуs	Met	Ala	Met	.Val		Ser	Arg	Leu	
20	Hig	Gln			T.au	Dho	C - ~	200	0		~-	_	205	_			
		210	- 7 -	TYL	neu	Phe	215	HIS	ser	Asn	GIA		Tyr	Tyr	Asp	Ser	
	Lvs			G3 11	Val	Ala			7 011	T	a1	220			_	_	
	225				• • • •	230	GIY	PHE	neu	ren	235	Inr	Pro	val	Lys		
	Thr	Arq	Ile	Ser	Ser	Pro	Phe	Ser	Tur	Glaz		Dho	wia	Dwa	37a 7	240	
25		•			245				- 7 -	250	AL 9	FIIG	птэ		.255	Leu	
	Lys	Val	Lys	Arg	Pro	His	Tvr	Glv	Val		Tvr	Δla	בומ	Laze	. 433 . U i a	Cl v	
				260			4 -	1	265		-1-		n_u	270	птэ	GLY	
	Ser	Leu	Ile	His	Ser	Ala	Ser	Asp	Gly	Arg	Val	Glv	Phe	Tle	Glv	Va l	
			275					280	-				285				
30	Lys	Ala	Gly	Tyr	Gly	Lys	Val	Val	Glu	Ile	His	Leu	Asn	Glu	Leu	Arg	
		290					295					300					
	Leu	Val	Tyr	Ala	His	Met	Ser	Ala	Phe	Ala	Asn	Gly.	Leu	Lys	Lys	Gly	
	305					310					315					320	
35	Ser	Phe	Val	Lys	Lys	Gly	Gln	Ile	Ile	Gly	Arg	Val	Gly	Ser	Thr	Gly	
33	•	<b>.</b>			325	· .				330					335		
	ьeu	ser	Tnr	GIA	Pro	His	Leu	His	Phe	Gly	Val	Tyr	Lys	Asn	Ser	Arg	
	D	T7 -		340	-		_		345					350			
	PIO	TTE	355	PIO	Leu	Gly	Tyr		Arg	Thr	Ala	Lys		Lys	Leu	His	
40	GI v	T 2.5		T. seem		77- 7	-1	360					365				
. 10	GLY	370	GIII	Arg	GIu	Val	Pne	Leu	GLu	Lys	Ala		Tyr	Ser	Lys	Gln	
·.	Ive			GI.	T.c.	Dho	375	mъ	TT 2 -	•	-1	380	_	_			
	385	u	بس	Jau	TEU	Phe 390	ьys	inr	HIS	ser		Glu	Lys	Asn	Ser		
		Leu	Leu	Glv	Glv						395					400	
45	.7.4.	4		J_4	405	- 11C											
	,						٠										

# (2) INFORMATION FOR SEQ ID NO:111:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 296 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

```
(iii) HYPOTHETICAL: YES
(vi) ORIGINAL SOURCE:
```

(A) ORGANISM: Helicobacter pylori

5

#### (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...296

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

Asp Tyr Glu Val Phe Ser Glu Thr Ile Phe Leu Gln Asn Met Val Tyr 50 55 60

20 Gln Pro Ile Glu Glu Arg Asn Ala Phe Phe Gln Leu Thr Lys Asp Glu 65 70 75 80

Asp Asn Ser Phe Asn Pro Glu Asn Ser Val Ile Leu Leu Asn Glu Pro 85 90 95

Ser Asp Asn Ser Glu Lys Asn Leu Leu Ser Tyr Pro Asn Asp Pro Asn 25 100 105 110

Asn Asn Glu Asp Asn Ala Asn Asn Ser Gln Lys Asn Pro Phe Leu Tyr 115 120 125

Lys Pro Lys Arg Lys Thr Lys Asn Pro Lys Leu Ile Glu Tyr Ser Gln 130 135 140

30 Gln Asp Phe Tyr Pro Leu Lys Asn Gly Asp Ile Ile Met Ser Lys Glu
145 150 155 160

Gly Asp Gln Trp Leu Ile Glu Ile Gln Ser Lys Ala Leu Lys Arg Phe 165 170 175

Leu Lys Asp Gln Asn Asp Lys Asp Arg Gln Ile Gln Thr Phe Thr Phe 35 180 185 190

Asn Asp Thr Lys Thr Gln Ile Ala Gln Ile Lys Gly Lys Ile Ser Ser 195 200 205

Tyr Val Tyr Thr Thr Asn Asn Gly Ser Leu Ser Leu Arg Pro Phe Tyr 210 215 220

Glu Ser Phe Leu Leu Glu Lys Lys Ser Asp Asn Val Tyr Thr Ile Glu 225 230 235 240

Asn Lys Ala Leu Asp Thr Met Glu Ile Ser Lys Cys Gln Met Val Leu 245 250 255

Lys Lys His Ser Thr Asp Lys Leu Asp Ser Gln His Lys Ala Ile Ser 45 260 265 270

Ile Asp Leu Asp Phe Lys Lys Glu Arg Phe Lys Ser Asp Thr Glu Leu 275 280 285

Phe Leu Glu Cys Leu Lys Glu Ser 290 295

50

55

#### (2) INFORMATION FOR SEQ ID NO:112:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 248 amino acids

(B) TYPE: amino acid

```
(D) TOPOLOGY: linear
```

- (ii) MOLECULE TYPE: protein
- 5 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori
- 10 (ix) FEATURE:

50

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...248
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:
- Val Ser Tyr Asp Asn Thr Asp Asp Tyr Tyr Phe Pro Arg Asn Gly Val

Ile Phe Ser Ser Tyr Ala Thr Met Ser Gly Leu Pro Ser Ser Gly Thr

Leu Asn Ser Trp Asn Gly Leu Gly Gly Asn Val Arg Asn Thr Lys Val 20

Tyr Gly Lys Phe Ala Ala Tyr His His Leu Gln Lys Tyr Leu Leu Ile

Asp Leu Ile Ala Arg Phe Lys Thr Gln Gly Gly Tyr Ile Phe Arg Tyr 25 70 75 Asn Thr Asp Asp Tyr Leu Pro Leu Asn Ser Thr Phe Tyr Met Gly Gly

90 Val Thr Thr Val Arg Gly Phe Arg Asn Gly Ser Ile Thr Pro Lys Asp

- 100 105 30
- Glu Phe Gly Leu Trp Leu Gly Gly Asp Gly Ile Phe Thr Ala Ser Thr 120

Glu Leu Ser Tyr Gly Val Leu Lys Ala Ala Lys Met Arg Leu Ala Trp 135

Phe Phe Asp Phe Gly Phe Leu Thr Phe Lys Thr Pro Thr Arg Gly Ser 35 150 155

Phe Phe Tyr Asn Ala Pro Thr Thr Thr Ala Asn Phe Lys Asp Tyr Gly 165 170 Val Val Gly Ala Gly Phe Glu Arg Ala Thr Trp Arg Ala Ser Thr Gly

185 Leu Gln Ile Glu Trp Ile Ser Pro Met Gly Pro Leu Val Leu Ile Phe

200 Pro Ile Ala Phe Phe Asn Gln Trp Gly Asp Gly Asn Gly Lys Lys Cys 215 220

Lys Gly Leu Cys Phe Asn Pro Asn Met Asn Asp Tyr Thr Gln His Phe 45 230 235

Glu Phe Ser Met Gly Thr Arg Phe

- (2) INFORMATION FOR SEQ ID NO:113:
  - (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 335 amino acids
    - (B) TYPE: amino acid
- (D) TOPOLOGY: linear 55

												-				
		(ii	) MO	LECU	LE T	YPE:	pro	tein			-					
		(iii	) ну	POTH	ETIC	AL:	YES									
5		(vi	•		AL S RGAN			icob	acte	r py	lori					
10			(	B) L	AME/ OCAT	ION	1	335								
					CE D											
15	Val 1	GIn	His	Phe	Asn 5	Phe	Leu	Tyr	Lys	Asp 10	Ser	Leu	Phe	Ser	Ile 15	Ala
				20	Ile				25					30		_
•	Ala	Tyr	Phe 35	Thr	Arg	Lys	Arg	Asn 40	Lys	Lys	Phe	Leu	Gln 45	Lys	Phe	Ala
20		50			Ala		55					60				
	65				Ile	70					75					80
25					Glu 85					90				•	95	
	Arg	Pro	Leu	Lys 100	Asp	Glu	Glu	Lys	Ile 105	Ala	Val	Leu	Asp	Leu 110	Leu	Ala
	Lys	Asn	Tyr 115	Phe	Ser	Val	Gly	Tyr 120	Leu	Gln	Lys	Thr	Lys 125	Asp	Thr	Val
30	Lys	Glu 130	Ile	Leu	Arg	Phe	Ser 135	Pro	Arg	Asn	Val	Glu 140	Ala	Leu	Leu	Lys
٠	Leu 145	Leu	His	Ala	Tyr	Glu 150	Leu	Glu	Lys	Asp	Tyr 155		Lys	Ala	Leu	Glu 160
35	Thr	Leu	Glu	Cys	Leu 165	Glu	Glu	Leu	Glu	Val 170	Pro	Lys	Ile	Glu	Thr 175	
	Lys	Asn	Tyr	Leu 180	Tyr	Leu	Met	His	Leu 185	Ile	Glu	Asn	Lys	Glu 190	Asp	Ala
	Ala	ГÀЗ	Ile 195	Leu	His	Val	Ser	Lys 200	Ala	Ser	Leu	Asp	Leu 205	Lys	Lys	Ile
40	Ala	Leu 210	Asn	His	Leu	Lys	Ser 215	His	Asp	Glu	Asn	Leu 220	Phe	Trp	Gln	Glu
	Ile 225	Asp	Thr	Thr	Glu	Arg 230	Leu	Glu	Asn	Va1	Ile 235	Asp	Leu	Leu	Trp	Asp 240
45	Met	Asn	Ile	Pro	Ala 245	Phe	Ile	Leu	Glu	Lys 250	His	Ala	Leu	Leu	Gln 255	
	Ile	Ala	Arg	Ser 260	Gln	Gly	Leu	Leu	Leu 265		His	Lys	Pro	Cys 270		Ile
	Phe	Glu	Leu 275	Glu	Val	Leu	Arg	Ala 280	Leu	Leu	His	Ser	Pro 285		Lys	Ala
50	Ser	Leu	Thr	Phe	Glu	Tyr	Arg		Lys	His	Cys	Lys		Ile	Phe	Pro

Phe Glu Ser His Arg Cys Pro Val Cys Tyr Gln Leu Ala Phe Met Asp

Met Val Leu Lys Ile Ser Lys Lys Thr His Ala Met Gly Val Asp

```
(2) INFORMATION FOR SEQ ID NO:114:
           (i) SEQUENCE CHARACTERISTICS:
 5
                (A) LENGTH: 413 amino acids
                (B) TYPE: amino acid
                (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
10
         (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
15
         (ix) FEATURE:
               (A) NAME/KEY: misc_feature
                (B) LOCATION 1...413
20
         (xi) SEQUENCE DESCRIPTION: SEO ID NO:114:
     Met Arg Lys Ile Phe Ser Tyr Ile Ser Lys Val Leu Leu Phe Ile Gly
                                         10
     Val Val Tyr Ala Glu Pro Asp Ser Lys Val Glu Ala Leu Glu Gly Arg
25
                                     25
     Lys Gln Glu Ser Ser Leu Asp Lys Lys Ile Arg Gln Glu Leu Lys Ser
                                 40
     Lys Glu Leu Lys Asn Lys Glu Leu Lys Asn Lys Asp Leu Lys Asn Lys
                             55
     Glu Glu Lys Lys Glu Thr Lys Ala Lys Arg Lys Pro Arg Ala Glu Val
30
                         70
                                             75
     His His Gly Asp Ala Lys Asn Pro Thr Pro Lys Ile Thr Pro Pro Lys
     Ile Lys Gly Ser Ser Lys Gly Val Gln Asn Gln Gly Val Gln Asn Asn
35
                                     105
     Ala Pro Lys Pro Glu Glu Lys Asp Thr Thr Pro Gln Ala Thr Glu Lys
                                 120
     Asn Lys Glu Thr Ser Pro Ser Ser Gln Phe Asn Ser Ile Phe Gly Asn
                             135
    Pro Asn Asn Ala Thr Asn Asn Thr Leu Glu Asp Lys Val Val Gly Gly
40
                         150
                                             155
     Ile Ser Leu Leu Val Asn Gly Ser Pro Ile Thr Leu Tyr Gln Ile Gln
                                         170
     Glu Glu Gln Glu Lys Ser Lys Val Ser Lys Ala Gln Ala Arg Asp Arg
45
                                     185
     Leu Ile Ala Glu Arg Ile Lys Asn Gln Glu Ile Glu Arg Leu Lys Ile
                                 200
     His Val Asp Asp Asp Lys Leu Asp Gln Glu Met Ala Met Met Ala Gln
                             215
50
    Gln Gln Gly Met Asp Leu Asp His Phe Lys Gln Met Leu Met Ala Glu
                         230
                                             235
```

Gly His Tyr Lys Leu Tyr Arg Asp Gln Leu Lys Glu His Leu Glu Met

Gln Glu Leu Leu Arg Asn Ile Leu Leu Thr Asn Val Asp Thr Ser Ser

265

	GIU	1111	275	Mec	Arg	GIU	Tyr	280		гÀг	HIS	ьуs	285		Pne	ser
	Ile	Pro	Thr	Glu	Ile	Glu	Thr			Tyr	Thr	Ser			Gln	Glu
5	<b>3</b>	290	<b>a</b> z	3			295	_	_	_	_	300		_		
<b>J</b>	305		GIU	Arg	ALA	Met 310	Ата	Asp	Pro	Asn	Leu 315	GIu	Val	Pro	Gly	Val 320
			Ala	Asn	Glu		Ile	Glu	Met	Lvs	Thr	Leu	Asn	Pro	Gln	
					325					330					335	
10	Ala	Gln	Val	Phe 340		Ser	His	Glu	Gln 345	Gly	Ser	Phe	Thr	Pro 350	Val	Met
	Asn	Gly	Gly 355	Gly	Gly	Gln	Phe	Ile 360		Phe	Tyr	Ile	Lys 365	Glu	Lys	Arg
	Gly	Lys 370	Asn	Glu	Val	Ser	Phe 375		Gln	Ala	Lys	Gln 380	Phe	Ile	Ala	Gln
15		Leu	Val	Glu	Glu		Lys	Asp	Lys	Ile	Leu	Glu	Glu	His	Phe	Glu
	385		7	17-3		390	•	-1-	1		395	_				400
	Lys	Leu	Arg	vai	Lys 405	ser	Arg	ile	Val	Met 410	Ile	Arg	Glu	-		
20	(2)	INF	ORMA!	rion	FOR	SEQ	ID I	NO:1	15:							
		(i)				HARA										
									acio	ds					٠.	
25						amiı OGY:										
		(ii)			٠	YPE:										
		(iii)					•									
30		, ,				<b>.</b> .	100									
		(vi)				OURCI		•								
			(2	A) OI	RGANI	ISM:	Hel:	icoba	acte	r py:	lori					
		(ix)	FE.	ATURI	3:											
35		,				KEY:	mis	_fea	ature	<b>e</b>						
			(1	3) L(	CAT	CON :	ι:	186								
		(xi)	SEÇ	QUENC	CE DE	ESCR	IPTIC	ON: S	SEQ :	ID NO	0:11	5:				÷
Ю	Met	Ile	Lys	Arq	Ile	Ala	Cys	Ile	Leu	Ser	Leu	Ser	Ala	Ser	Leu	Ala
	1		•		5					10					15	
	Leu	Ala	Gly	Glu 20	Val	Asn	Gly	Phe	Phe 25	Met	Gly	Ala	Gly	Tyr 30	Gln	Gln
15	Gly	Arg	Tyr 35	Gly	Pro	Tyr	Asn	Ser 40	Asn	Tyr	Ser	Asp	Trp 45	Arg	His	Gly
		Asp 50	Leu	Tyr	Gly	Leu	Asn 55		Lys	Leu	Gly	Phe 60		Gly	Phe	Ala
	Asn 65	Lys	Trp	Phe	Gly	Ala 70	Arg	Val	Tyr	Gly	Phe	Leu	Asp	Trp	Phe	Asn 80
0		Ser	Gly	Thr			Thr	Lys	Thr		Leu	Leu	Thr	Tyr		Gly
	Gly	Gly	Asp	Leu	85 Ile	Val	Asn	Leu	Ile	90 Pro	Leu	Asp	Lys	Phe	95 Ala	
	<b>63</b>	T	T1 -	100	<b>a</b> 1	17. 3	<b>01</b>	7	105	<b>a</b> 2 -		m)	<b></b>	110	<b>5</b> 1.	_
5	GTA	neu	11e	σтλ	σтλ	val	GIU	120	ATA	стЛ	Asn	rnr	125	met	hue	Pro

55

```
- 190 -
     Tyr Asp Val Asn Gln Thr Arg Phe Gln Phe Leu Trp Asn Leu Gly Gly
                              135
     Arg Met Arg Val Gly Asp Arg Ser Ala Phe Glu Ala Gly Val Lys Phe
                         150
                                              155
     Pro Met Val Asn Gln Gly Ser Lys Asp Val Gly Leu Ile Arg Tyr Tyr
                     165
                                          170
     Ser Trp Tyr Val Asp Tyr Val Phe Thr Phe
                 180
10
     (2) INFORMATION FOR SEQ ID NO:116:
          (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 242 amino acids
                (B) TYPE: amino acid
15
                (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
        (iii) HYPOTHETICAL: YES
20
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
25
               (A) NAME/KEY: misc_feature
               (B) LOCATION 1...242
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:
30
     Met Lys Lys Phe Phe Ser Gln Ser Leu Leu Ala Leu Ile Ile Ser Met
                                          10
     Asn Ala Val Ser Gly Met Asp Gly Asn Gly Val Phe Leu Gly Ala Gly
                                      25
     Tyr Leu Gln Gly Gln Ala Gln Met His Ala Asp Ile Asn Ser Gln Lys
35
                                 40
     Gln Ala Thr Asn Ala Thr Ile Lys Gly Phe Asp Ala Leu Leu Gly Tyr
                            55
     Gln Phe Phe Phe Glu Lys His Phe Gly Leu Arg Leu Tyr Gly Phe Phe
                         70
     Asp Tyr Ala His Ala Asn Ser Ile Lys Leu Lys Asn Pro Asn Tyr Asn
                                          90
     Ser Glu Ala Ala Gln Val Ala Ser Gln Ile Leu Gly Lys Gln Glu Ile
                                     105
     Asn Arg Leu Thr Asn Ile Ala Asp Pro Arg Thr Phe Glu Pro Asn Met
45
                                 120
```

Leu Thr Tyr Gly Gly Ala Met Asp Val Met Val Asn Val Ile Asn Asn

Gly Ile Met Ser Leu Gly Ala Phe Gly Gly Ile Gln Leu Ala Gly Asn

Ser Trp Leu Met Ala Thr Pro Ser Phe Glu Gly Ile Leu Val Glu Gln

Ala Leu Val Ser Lys Lys Ala Thr Ser Phe Gln Phe Leu Phe Asn Val 180 185 190 Gly Ala Arg Leu Arg Ile Leu Lys His Ser Ser Ile Glu Ala Gly Val

200

155

170

#### (2) INFORMATION FOR SEQ ID NO:117:

- 10 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 256 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 15 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
- 20 (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc\_feature
    - (B) LOCATION 1...256
- 25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

Met Gly Tyr Ala Ser Lys Leu Ala Leu Lys Ile Cys Leu Val Gly Leu

1 5 10 15

30 Cys Leu Phe Ser Thr Leu Gly Ala Glu His Leu Gly Gly Lys Gly Asp

Organ 20 Cys Leu Phe Ser Thr Leu Gly Ala Glu His Leu Glu Gln Lys Gly Asn 20 25 30

Tyr Ile Tyr Lys Gly Glu Glu Ala Tyr Asn Asn Lys Glu Tyr Glu Arg 35 40 45

Ala Ala Ser Phe Tyr Lys Ser Ala Ile Lys Asn Gly Glu Ser Leu Ala
55 60

Tyr Ile Leu Leu Gly Ile Met Tyr Glu Asn Gly Arg Gly Val Pro Lys 65 70 75 80

Asp Tyr Lys Lys Ala Val Glu Tyr Phe Gln Lys Ala Val Asp Asn Asp 85 90 95

40 Ile Pro Arg Gly Tyr Asn Asn Leu Gly Val Met Tyr Lys Glu Gly Lys
100 105 110

Gly Val Pro Lys Asp Glu Lys Lys Ala Val Glu Tyr Phe Arg Ile Ala 115 120 125

Thr Glu Lys Gly Tyr Thr Asn Ala Tyr Ile Asn Leu Gly Ile Met Tyr 45 130 135 140

Met Glu Gly Arg Gly Val Pro Ser Asn Tyr Ala Lys Ala Thr Glu Cys 145 150 155 160

Phe Arg Lys Ala Met His Lys Gly Asn Val Glu Ala Tyr Ile Leu Leu

165 170 175

50 Gly Asp Ile Tyr Tyr Ser Gly Asn Asp Gln Leu Gly Ile Glu Pro Asp
180 185 190

Lys Asp Lys Ala Val Val Tyr Tyr Lys Met Ala Ala Asp Val Ser Ser 195 200 205

Ser Arg Ala Tyr Glu Gly Leu Ser Glu Ser Tyr Arg Tyr Gly Leu Gly 55 210 215 220

225

240

•	Va]	. Gli	ı Lys	s Asp	Lys	230		Ala	Glu	ı Glu	Tyr 235		Glr	Lys	Ala	Cys 240
	Asp	Phe	Asp	) Ile	245	Lys	Asr	Cys	Lys	Lys 250	Lys		Thr	Ser	Ser 255	Arg
5																
	(2)	INI	ORMA	MOITA	FOR	SEC	DID	NO:1	18:			٠				,
•		( j	.) SE	OUEN	ICE C	HARA	CTER	TSTT	CS.							
		• -			ENGI					.ds						
10					YPE:											
				(D) I	OPOL	OGY:	lin	lear							•	
		(ii	.) MC	LECU	LE T	YPE:	pro	tein	,		•					
15		(iii	.) HY	POTH	ETIC	AL:	YES					No.	•		٠	
		(vi			IAL S											
			(	(A) C	RGAN	ISM:	Hel	icob	acte	r py	lori					
20		(ix	) FE	ATTIR	E.											
			-		AME/	KEY:	mis	c_fe	atur	е						
		1	(	B) L	OCAT	ION	1	657						•		
		(xi	) SE	OHEN	CE D	ESCD	TOTT	ON.	CEO.	TD N	0-11	٥.				
25	•	,						OIV.	SEQ	ID N	0:11	0:				
	Met	Arg	Lys	Leu		Ile	Pro	Leu	Leu	Leu	Phe	Ser	Ala	Leu	Glu	Ala
	1 Asn	Glu	Lvs	Asn	ี 5 เสาษ	Phe	Dhe	Tle	G3···	10	<b>~</b> 1	nh e	<b>01</b>	Thr	15	•
				20					25					30		
30	Leu	Glu	Gly	Thr	Gln	Thr	Gln		Lys	Arg	His	Thr	Thr	Thr	Lys	Asn
	Thr	Tvr	35 Ala	Thr	Tvr	Asn	Tvr	40 Len	Pro	Thr	y e.b.	The	45	Leu	T	3
		50					55					60				
35	Ala	Ala	Asn	Leu	Phe		Asn	Ala	Glu	Ala	Ile	Ser	Lys	Leu	Lys	Phe
35	65 Ser	Ser	Leu	Ser	Pro	70 Val	Ara	17-1	Loui	Tra san	75 Mor	TD:		Gly	~1	80
					85	V41	Arg	val	neu	90	Mec	Tyr	ASN	GTÄ	95	Leu
	Thr	Ile	Glu	Asn	Phe	Leu	Pro	Tyr	Asn	Leu	Asn	Asn	Val	Lys	Leu	Ser
40	Phe	Thr	Asp	100	Gln	Glv	λαn	17-1	105	X	T	<b>a</b> 1	**- 7	110 Ile		_,
			115					120					125			
	Ile	Pro	Lys	His	Ser	Lys	Ile	Val	Leu	Pro	Gly	Glu	Ala	Phe	Asp	Ser
		130					135					140				
45	145	275	110	nap	110	150	1111	. Leu	Pne	Leu	155	rys	IIe	Glu	Ala	Thr 160
	Ser	Thr	Ser	Ile	Ser	Asp	Ala	Asn	Thr	Gln		Val	Phe	Glu	Thr	Leu
					165					170					175	
	ASII	nys	TTE	180	Im	ASI	ren	vaı	Val 185	Asn	Tyr	Arg	Asn	Glu	Asn	Lys
50	Phe	Lys	Asp		Glu	Așn	His	Trp		Ala	Phe	Thr	Pro	190 Gln	Thr	Ala
			195					200					205			
	GLU	210	rne	inr	Asn	ren	Met 215	Leu	Asn	Met	Ile	Ala 220	Val	Leu	Asp	Ser
	Gln		Trp	Gly	Asp	Ala		Leu	Asn	Ala	Pro	Phe	Glu	Phe	Thr	Asn

WO 98/18323 PCT/US97/19575

- 193 -

	Ser	Pro	Thr	Asp	Cys 245	Asp	Asn	Asp	Pro	Ser 250	Lys	Суз	Val	Asn	Pro 255	Gly
	Thr	Asn	Gly	Leu 260	Val	Asn	Ser	Lys	Val 265	Asp	Gln	Lys	Tyr	Val 270	Leu	Asn
5	Lys	Gln	Asp 275	Ile	Val	Asn	Lys	Phe 280	Lys	Asn	Lys	Ala	Asp 285		Asp	Val
	Ile	Val 290	Leu	Lys	Asp	Ser	Gly 295	Val	Val	Gly	Leu	Gly 300	Ser	Asp	Ile	Thr
10	Pro 305	Ser	Asn	Asn	Asp	Asp 310	Gly	Lys	His	Tyr	Gly 315	Gln	Leu	Gly	Val	Val 320
	Ala	Ser	Ala	Leu	Asp 325	Pro	Lys	Lys	Leu	Phe 330	Gly	Asp	Asn	Leu	Lys 335	Thr
	Ile	Asn	Leu	Glu 340	Asp	Leu	Arg	Thr	Ile 345	Leu	His	Glu	Phe	Ser 350	His	Thr
15	Lys	Gly	Tyr 355	Gly	His	Asn	Gly	Asn 360		Thr	Tyr	Gln	Arg 365	Val	Pro	Val
	Thr	Lys 370	Asp	Gly	Gln	Val	Glu 375	Lys	Asp	Ser	Asn	Gly 380	Lys	Pro	Lys	Asp
20	Ser 385	Asp	Gly	Leu	Pro	Tyr 390	Asn	Val	Cys	Ser	Leu 395	Tyr	Gly	Gly	Ser	Asn 400
	Gln	Pro	Ala	Phe	Pro 405	Ser	Asn	Tyr	Pro	Asn 410	Ser	Ile	Tyr	His	Asn 415	Cys
	Ala	Asp	Val	Pro 420	Ala	Gly	Phe	Leu	Gly 425	Val	Thr	Ala	Ala	Val 430	Trp	Gln
25			Ile 435					440				-	445			-
		450	Thr				455					460				
30	465		Ser			470				-	475					480
			Asn		485					490				_	495	
2.5			Gly	500					505	-			_	510		
35			Gly 515				•	520					525			
		530	Asn				535					540				
40	545		Leu			550					555					560
			Gln		565					570			_		575	
45			Arg	580					585					590		
40			Gly 595		•		-	600					605			
		610	Lys				615					620				_
50	625		Val			630					635					640
		GIU	Gly	ATA	Ser 645	HIS	rne	пÀŝ	vaı	Phe 650	rue	ASN	Tyr	атХ	1rp 655	val
	Phe							•								

45

50

```
(2) INFORMATION FOR SEQ ID NO:119:
```

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 167 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- 10 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

- 15 (ix) FEATURE:
  - (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...167
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

20 Met Lys Leu Val Ser Leu Ile Val Ala Leu Val Phe Cys Cys Phe Leu

Gly Ala Val Glu Leu Pro Gly Val Tyr Gln Thr Gln Glu Phe Leu Tyr

20 25 30 25 Met Lys Ser Ser Phe Val Glu Phe Phe Glu His Asn Gly Lys Phe Tyr

25 Met Lys Ser Ser Phe Val Glu Phe Phe Glu His Asn Gly Lys Phe Tyr
35 40 45

Ala Tyr Gly Ile Ser Asp Val Asp Gly Ser Lys Ala Lys Lys Asp Lys 50 55 60

Phe Leu Ser Asp Leu Ile Lys Val Gly Glu Gln Ser Tyr Lys Gly Gly 85 90 95

Lys Ala Tyr Asn Phe Tyr Asp Gly Lys Thr Tyr His Val Arg Val Thr 100 105 110

35 Gln Asn Ser Asn Gly Asp Leu Glu Phe Thr Ser Ser Tyr Asp Lys Trp
115 120 125

Gly Tyr Val Gly Lys Thr Phe Thr Trp Lys Arg Leu Ser Asp Glu Glu 130 135 140

40 Ile Lys Asn Leu Lys Leu Lys Arg Phe Asn Leu Asp Glu Val Leu Lys Arg Phe Asn Leu Asp Glu Val Leu Lys Lys Leu Lys Lys Asp Ser Pro Ile

165

(2) INFORMATION FOR SEQ ID NO:120:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 294 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

- (iii) HYPOTHETICAL: YES
- 55 (vi) ORIGINAL SOURCE:

#### (A) ORGANISM: Helicobacter pylori

#### (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- 5 (B) LOCATION 1...294

#### (xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

- Met Ser Asn Gln Ala Ser His Leu Asp Asn Phe Met Asn Ala Lys Asn 10 Pro Lys Ser Phe Phe Asp Asn Lys Gly Asn Thr Lys Phe Ile Ala Ile Thr Ser Gly Lys Gly Gly Val Gly Lys Ser Asn Ile Ser Ala Asn Leu 15 Ala Tyr Ser Leu Tyr Lys Lys Gly Tyr Lys Val Gly Val Phe Asp Ala Asp Ile Gly Leu Ala Asn Leu Asp Val Ile Phe Gly Val Lys Thr His 75 Lys Asn Ile Leu His Ala Leu Lys Gly Glu Ala Lys Leu Gln Glu Ile 20 85 90 Ile Cys Glu Ile Glu Pro Gly Leu Cys Leu Ile Pro Gly Asp Ser Gly 100 105 Glu Glu Ile Leu Lys Tyr Ile Ser Gly Ala Glu Ala Leu Asp Arg Phe 120 25 Val Asp Glu Glu Gly Val Leu Ser Ser Leu Asp Tyr Ile Val Ile Asp 135 140 Thr Gly Ala Gly Ile Gly Ala Thr Thr Gln Ala Phe Leu Asn Ala Ser 155 Asp Cys Val Val Ile Val Thr Thr Pro Asp Pro Ser Ala Ile Thr Asp 30 165 170 Ala Tyr Ala Cys Ile Lys Ile Asn Ser Lys Asn Lys Asp Glu Leu Phe Leu Ile Ala Asn Met Val Ala Gln Pro Lys Glu Gly Arg Ala Thr Tyr 35 Glu Arg Leu Phe Lys Val Ala Lys Asn Asn Ile Ala Ser Leu Glu Leu 215 His Tyr Leu Gly Ala Ile Glu Asn Ser Ser Leu Leu Lys Arg Tyr Val 230 235 Arg Glu Arg Lys Ile Leu Arg Lys Ile Ala Pro Asn Asp Leu Phe Ser 40 245 250 Gln Ser Ile Asp Gln Ile Ala Ser Leu Leu Val Ser Lys Leu Glu Thr 265 Gly Thr Leu Glu Ile Pro Lys Glu Gly Leu Lys Ser Phe Phe Lys Arg 280 45 Leu Leu Lys Tyr Leu Gly . 290
  - (2) INFORMATION FOR SEQ ID NO:121:
- 50 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 372 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 55 (ii) MOLECULE TYPE: protein

```
(iii) HYPOTHETICAL: YES
```

# (vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

### (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...372

10

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

			.,	, <u>v</u> O L L		LIDCE	TETT	.OIV:	SEQ	TD V	10:12	1:				
	Lev	Glu	ı Pro	Ser	Arg	Asn	Arc	1 Leu	Lva	His	בומ:	λ1 <b>-</b>	Dhe	Dho	37-1	Gly
	Τ.				5					10					15	
15				20					25					30	Ser	Pro
			35					40					45			Tyr
20		50					55					60				His
	65					70					75					Tyr 80
0.5					85					90					95	Asn
25				100				Arg	105					110		
			TTO					120			-		125			Leu
30		130					135	His				140				
	145					1.50		Trp			155					160
25					165			His		170					175	
35				180				Ser	185					190		
			195					Met 200					205			
40		210					215	Lys				220				
	225					230		Leu			235					240
AE					245			Val		250					255	
45				26U				Thr	265					270		
			2/5					Lys 280					285			
50		290					295	Tyr				300				
	Ser	Leu	Arg	Arg	Lys	Glu	Leu	Trp	Leu	Ser		Leu	Glu	Asn	Ser	Asn
		Phe	Lvs	Thr	Leu	310 Lvs	Va 1	Len	λ c.∽	T	315	3	<b>6</b> 3		_	320
55					325			Leu		330					225	
55	Pro	ser	Tyr	Ser	Leu	Asn	Pro	His	Phe	Ile	Asp	Ile	Val	Tyr	Thr	Tyr

- 197 -

```
345
     Asn Arg Ser His Ile Lys His Ile Arg Phe Asn Met Ala Tyr Leu Asn
                                  360
     Ser Leu Leu Lys
 5
         370
     (2) INFORMATION FOR SEQ ID NO:122:
          (i) SEQUENCE CHARACTERISTICS:
10
               (A) LENGTH: 978 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
15
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
20
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...978
25
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:
     Met Lys Lys Arg Lys His Val Ser Lys Lys Val Phe Asn Val Ile Ile
     Leu Phe Val Ala Val Phe Thr Leu Leu Val Val Ile His Lys Thr Leu
30
     Ser Asn Gly Ile His Ile Gln Asn Leu Lys Ile Gly Lys Leu Gly Ile
                                 40
     Ser Glu Leu Tyr Leu Lys Leu Asn Asn Lys Leu Ser Leu Glu Val Glu
                             55
     Arg Val Asp Leu Ser Ser Phe Phe His Gln Lys Pro Thr Lys Lys Arg
     Leu Glu Val Ser Asp Leu Ile Lys Asn Ile Arg Tyr Gly Ile Trp Ala
     Val Ser Tyr Phe Glu Lys Leu Lys Val Lys Glu Ile Ile Leu Asp Asp
40
                                     105
     Lys Asn Lys Ala Asn Ile Phe Phe Asp Gly Asn Lys Tyr Glu Leu Glu
                                 120
     Phe Pro Gly Ile Lys Gly Glu Phe Ser Leu Glu Asp Asp Lys Asn Ile
                             135
45
     Lys Leu Lys Ile Ile Asn Leu Leu Phe Lys Asp Val Lys Val Gln Val
                                             155
     Asp Gly Asn Ala His Tyr Ser Pro Lys Ala Arg Lys Met Ala Phe Asn
                                         170
    Leu Ile Val Lys Pro Leu Val Glu Pro Ser Ala Ala Ile Tyr Leu Gln
50
                                     185
                                                         190
     Gly Leu Thr Asp Leu Lys Thr Ile Glu Leu Lys Ile Asn Thr Ser Pro
                                 200
                                                   205
    Met Lys Ser Leu Ala Phe Leu Lys Pro Leu Phe Gln Arg Gln Ser Gln
                             215
                                                 220
    Lys Asn Leu Lys Thr Trp Ile Phe Asp Lys Ile Gln Phe Ala Ser Phe
55
```

	225	5				.230	)				235					240
	Lys	; Ile	e Asr	Asr	Ala 245	Leu	Ile	Lys	Ala	Asr 250	Phe		Pro	Ser	Glu 255	Phe
5	Ile	Pro	Ser	Leu 260	Leu	Glu	Asr	Ser	Val 265	. Val	. Lys	. Ala	Thr	Leu 270	lle	Lys
	Pro	Sei	val 275	. Val	Phe	Asn	Asp	Gly 280	Leu		Pro	Ile	Lys 285	Met	Asp	Lys
	Thr	Gli 290	ı Lev	lle	Phe	Lys	Asn 295	Lys		Lev	. Leu	Ile 300	Gln	Pro	Gln	Lys
10	11e 305	Thi	Tyr	Glu	Thr	Met 310	Glu	Leu	Thr	Gly	Ser 315	Tyr	Ala	Thr	Phe	Ser 320
	Asn	Let	ı Leu	Glu	Ala 325	Pro	Lys	Leu	Glu	Val 330	Phe	Leu	Lys	Thr	Thr	Pro
15				340	'				345	Leu	Leu			350	Lys	Val
			355	•				360					365	Asp	Leu	Lys
•		370	)				375					380	Phe	Ser		Gln
20	385					390					395					Pro
- 1 .				Gln	405					410					415	
25				Tyr 420					425					430		
			435					440					445			
30		450		Leu			455					460				
30	465			Ser		470					475			,		480
				Leu	485					490					495	
35				Glu 500					505					510		
			515	Asp				520					525			
40		530		Ser			535					540				
	545			Ser		550					555					560
				Thr	565					570					575	
45				580 Asp			•		585					590		
			595	Pro				600					605			
50		910		Gly			615					620				
	625					630					635					640
				Ile	645					650	Asp				Ile 655	Thr
55	ren	Asn	Asn	Ile 660	Asp	Leu	Ser	Ile	Asp 665	Asp	Phe	Leu	Asp	Ser 670	Lys	Met

			675			Leu		680					685	_		
_		690				Asp	695					700				_
5	705					Lys 710					715					720
					725	Ile				730					735	
10				740		Gln			745				_	750		•
			755			Met		760					765		_	
		770				Ser	775					780				_
15	785					Gly 790			•		795					800
					805	Glu				810					815	
20				820		Asn			825					830		
			835			Asn		840			•		845			
		<b>85</b> 0				Val	855					860				
25	865					Val 870					875					880
					885	Lys				890					895	
30				900		Ser			905					910		
			915			Lys		920				•	925			
		930				Lys	935					940				
35	945					Phe 950					955					960
	Asp	Ile	Ile	Val	Asp 965	Glu	Val	Lys	Lys	Asn 970	Ile	qeA	Ser	Lys	Arg 975	Lys
40	Leu	Lys											•			ē

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 477 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

50

45 .

# (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...477

# 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

											_					
	_									าก						e Thi
10				20					25					20	e Ly	s Glr
								40					AE			o Pro
1.5							22					60				s Glu
15						, ,					76					s Ser 80
					00					90						r Thr
20				100	,				105	•					Met	: Lys
				,				120	)				125	Asr	Ala	a Ser
0.5			-				133	<b>)</b> .				7.40	Туг	Lys		Tyr
25						T20	,				. 166	Asn	Val			Gly
					103					170						Ser
30				100					185					7.00	Gln	Val
			~~~					200					205	Met	Ile	Ala
25							413					220				Thr
35						230					235	Asp	Leu			Leu 240
				Gly	243					250					255	Phe
40				Gln 260					755					0.00	Leu	
				Leu				280					205			
45		200		Gln			495					200				
43				Asn		310					71"					
				Leu						330						Arg
50				Phe 340					145					250		
				Ile				160					200	Lys		
55				Gly			313					Leu	Ala			
در	ren	GIU	GIn	Glu	Lys .	Asp	Glu	Gln	Leu	Tyr .	Arg	Lys	Ser	Leu	Asp	Ile

- 201 -

	385					390					395					400
				Lys	405					410					415	
5				Ala 420					425					430		
			435	Tyr				440					445			
		450		Leu			455					460	•	Ala	Asn	Tyr
10	11e 465	Phe	Asn	Ser	Gly	His 470	Lys	Ile	Asp	Asp	Tyr 475	Val	His			
	(2)	INF	ORMA'	TION	FOR	SEQ	ID <sub>.</sub>	NO:1	24:							
15		(i	() ()	QUENCA) L: B) T D) T	ENGT YPE :	H: 4: ami:	12 an	mino cid		ds						
20		(ii)	) MO:	LECU	LE T	YPE:	pro	tein								
		(iii	) HY	POTH	ETIC	AL: Y	YES									
25		(vi)		IGINA A) O				icoba	acte:	r py:	lori					
	•	(ix)	(2	ATURI A) N	AME/1			-	atur	<b>e</b> .						
30				B) L				•					٠			
				QUEN												
. ~	1			Phe	5					10					15	
35				Ala 20					25					30		
			35	Gln				40			•		45			
10		50		Leu			55					60				
	65			Lys		70					75					80
	Ala	Asn	Val	Ser	Asp 85	Phe	Phe	Arg	Leu	Asp 90	Ser	Thr	Leu	Met	Gln 95	Asn
15	Met	Ser	Leu	Gly 100	Leu	Ser	Gln	Lys	Val 105	Asp	Leu	Asn	Gly	Lys 110	Lys	Leu
	Thr	Gln	Ser 115	Lys	Met	Ile	Asn	Leu 120	Glu	Lys	Gln	Lys	Lys 125	Ile	Leu	Glu
0	Leu	Lys 130	Lys	Thr	Lys	Gln	Gln 135		Val	Ile	Asn	Leu 140		Ile	Asn	Gly
	145			Tyr		150					155	Leu			•	160
_	Ile	Lys	Asn	Leu	165		Thr	Leu	Tyr	Gln 170	Ala	Asn	His	Ser	Ser 175	Ser
5	Dane	3	*	<b>T1</b>	* 7 -	T1 ~	7.1 -	T	*			_	_		-	_

													100				
				180					185					190	)		
	Glu	Ile	Gln 195	Lys	Asn	Asp	Leu	Glu 200		Ala	Leu	Ser	Ser 205		His	Tyr	
5	Ser	Met 210	Gly	Glu	Leu	Thr	Phe 215	Lys	Glu	Asn	Glu	Ile 220	Leu	Ser	Ile	Ala	
-	Pro 225	Lys	Asn	Phe	Glu	Phe 230		Asn	Glu	Gln		Leu	His	Asn	Ile	Ser	
		Thr	Asn	Туг	Asp		Ala	Ile	Ala		235 Leu	Asp	Glu	Glu	Lys	240 Ala	
10	Gln	Lys	Asp	Ile	245 Thr	Leu	Ala	Lys	Lys	250 Ser	Phe	Leu	Glu	Asp	255 Ile	Asn	
				260					265					270		Asp	
			275					280					285			Gln	
15		290					295					300					
-	305					310					315					Ser 320	
					325					330					335	Leu	
20	Leu	Lys	ГÀЗ	Leu 340	Glu	Thr	Leu	Gln	Lys 345	Asn	Leu	Glu	Ser	Ile 350	Asn	Lys	
	Ile	Ile	Lys 355	Gln	Asn	Glu	Lys	Ile 360		Gln	Ile	Tyr		Leu	Asp	Leu	
25	Lys	Thr 370		Gly	Asp	Tyr	Asn 375		Tyr	Tyr	Asn		365 Leu	Asn	Asp	Lys	
	Ile		Ile	Gln	Ile	Thr		Leu	Glu	Thr	Leu	380 Ser	Ala	Leu	Asn	Ser	
	385 Ala	Tyr	Leu	Ser		390 Gln	Asn	Leu	Lys	Gly	395 Leu	Glu				400	
30					405					410							
	(2)	INFO	RMAT	NOI	FOR	SEQ	ID N	10:12	25 :								
		(i)		QUENC								•					
35			(E		PE:	amin	o ac	id	acıo	ls							
·			(I	) TC	POLO	GY:	line	ar									
		(ii)	MOI	ECUL	E TY	PE:	prot	ein									٠.
40	(	iii)	HYE	OTHE	TICA	L: Y	ES										
		(vi)		GINA													
A E				) OR		om:	неті	сора	cter	рλτ	ori						
45		(ix)		TURE ) NA		EY:	misc	_fea	ture								
			(B	) LO	CATI	ON 1	1	37	•	•							
50		(xi)	SEQ	UENC	E DE	SCRI	PTIO	N: S	EQ I	D NO	:125	:					. •
	Met .	Arg	Ile	Val .	Arg	Asn :	Leu	Phe			Ser	Phe	Val	Ala	Tyr	Ser	
	Ser .	Ala :	Phe	Ala.	ala :	Asp :	Leu	Glu		10 Gly	Thr	Lys	Asn	Asp	15 Lys	Lys	
55	Ser			20					25					30			
													-				

WO 98/18323 PCT/US97/19575

- 203 -

35 40 Glu Thr Lys Asn Asp Lys Lys Leu Tyr Asp Phe Thr Lys Asn Ser Gly 55 Leu Glu Gly Val Asp Leu Glu Lys Ser Pro Asn Leu Lys Ser His Lys 75 Lys Ser Asp Lys Lys Phe Tyr Lys Gln Leu Ala Lys Asn Asn Ile Ala Glu Gly Val Ser Met Pro Ile Val Asn Phe Asn Lys Ala Leu Ser Phe 105 Gly Pro Tyr Phe Glu Arg Thr Lys Ser Lys Lys Thr Gln Tyr Met Asp 120 Gly Gly Leu Met Met His Ile Arg Phe 15 (2) INFORMATION FOR SEQ ID NO:126: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 309 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: 30 (A) NAME/KEY: misc feature (B) LOCATION 1...309 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:126: 35 Leu Met Pro Gln Asn Gln Leu Val Ile Thr Ile Ile Asp Glu Ser Gly Ser Lys Gln Leu Lys Phe Ser Lys Asn Leu Lys Arg Asn Leu Ile Ile Ser Val Val Ile Leu Leu Leu Ile Val Gly Leu Gly Val Gly Phe Leu 40 40 Lys Phe Leu Ile Ala Lys Met Asp Thr Met Thr Ser Glu Arg Asn Ala 55 Val Leu Arg Asp Phe Arg Gly Leu Tyr Gln Lys Asn Tyr Ala Leu Ala 45 Lys Glu Ile Lys Asn Lys Arg Glu Glu Leu Phe Ile Val Gly Gln Lys Ile Arg Gly Leu Glu Ser Leu Ile Glu Ile Lys Lys Gly Ala Asn Gly 105 Gly His Leu Tyr Asp Glu Val Asp Leu Glu Asn Leu Ser Leu Asn 50 . 120 Gln Lys His Leu Ala Leu Met Leu Ile Pro Asn Gly Met Pro Leu Lys 135 140 Thr Tyr Ser Ala Ile Lys Pro Thr Lys Glu Arg Asn His Pro Ile Lys

155

Lys Ile Lys Gly Val Glu Ser Gly Ile Asp Phe Ile Ala Pro Leu Asn

```
170
     Thr Pro Val Tyr Ala Ser Ala Asp Gly Ile Val Asp Phe Val Lys Thr
                                      185
     Arg Ser Asn Ala Gly Tyr Gly Asn Leu Val Arg Ile Glu His Ala Phe
                                  200
     Gly Phe Ser Ser Ile Tyr Thr His Leu Asp His Val Asn Val Gln Pro
                             215
     Lys Ser Phe Ile Gln Lys Gly Gln Leu Ile Gly Tyr Ser Gly Lys Ser
                         230
10
     Gly Asn Ser Gly Gly Glu Lys Leu His Tyr Glu Val Arg Phe Leu Gly
     Lys Ile Leu Asp Ala Glu Lys Phe Leu Ala Trp Asp Leu Asp His Phe
     Gln Ser Ala Leu Glu Glu Asn Lys Phe Ile Glu Trp Lys Asn Leu Phe
15
                                  280
     Trp Val Leu Glu Asp Ile Val Gln Leu Gln Glu His Val Asp Lys Asp
                              295
     Thr Leu Lys Gly Gln
20
      (2) INFORMATION FOR SEQ ID NO:127:
           (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 332 amino acids
25
                (B) TYPE: amino acid
                (D) TOPOLOGY: linear
         (ii) MOLECULE TYPE: protein
30
        (iii) HYPOTHETICAL: YES
         (vi) ORIGINAL SOURCE:
               (A) ORGANISM: Helicobacter pylori
         (ix) FEATURE:
               (A) NAME/KEY: misc feature
               (B) LOCATION 1...332
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:
40
     Val Leu Tyr Phe Leu Thr Ser Leu Phe Ile Cys Ser Leu Ile Val Leu
                                         10
     Trp Ser Lys Lys Ser Met Leu Phe Val Asp Asn Ala Asn Lys Ile Gln
     Gly Phe His His Ala Arg Thr Pro Arg Ala Gly Gly Leu Gly Ile Phe
     Leu Ser Phe Ala Leu Ala Cys Tyr Leu Glu Pro Phe Glu Met Pro Phe
     Lys Gly Pro Phe Val Phe Leu Gly Leu Ser Leu Val Phe Leu Ser Gly
50
     Phe Leu Glu Asp Ile Asn Leu Ser Leu Ser Pro Lys Ile Arg Leu Ile
                                         90
     Leu Gln Ala Val Gly Val Val Cys Ile Ile Ser Ser Thr Pro Leu Val
                                     105
    Val Ser Asp Phe Ser Pro Leu Phe Ser Leu Pro Tyr Phe Ile Ala Phe
```

WO 98/18323 PCT/US97/19575

- 205 -

			115					120					125			
	Leu	Phe 130	Ala	Ile	Phe	Met	Leu 135	Val	Gly	Ile	Ser	Asn 140	Ala	Ile	Asn	Ile
. 5		Asp	Gly	Phe	Asn		Leu	Ala	Ser	Gly		Суз	Ala	Ile	Ala	
` 3	145	1	<b>-1</b> -	***	Th	150	<b>3</b>	D			155	<b>0</b>	<b>~</b>	<b>.</b>		160
	Leu				165					170					175	
	Tyr	Met	Val	Leu 180	Gly	Phe	Met	Val	Leu 185	Asn	Phe	Pro	Ser	Gly 190	Lys	Ile
10	Phe	Leu	Gly 195	Asp	Gly	Gly	Ala	Tyr 200	Phe	Leu	Gly	Leu	Val 205	Cys	Gly	Ile
	Ser	Leu 210	Leu	His	Leu		Leu 215	Glu	Gln	Lýs	Ile	Ser 220	Val	Phe	Phe	Gly
	Leu		Leu	Met	Leu			Val	Ile	Glu	Val		Phe	Ser	Ile	Leu
15	225					230					235					240
		Arg	Lys	Ile	Lys 245		Gln	Lys	Ala	Thr 250			Asp	Asn	Leu 255	Ḥis
	Leu	His	Thr	Leu 260		Phe	Lys	Phe	Leu 265		Gln	Arg	Ser	Phe 270		
20	Pro	Asn	Pro 275		Cys	Ala	Phe	Ile 280		Ile	Leu	Cys	Asn 285	Leu	Pro	Phe
	Ile			Ser	Val	Leu			Leu	Asp	Ala	-		Leu	Ile	Val
	Tla	290	T.011	· 17=1	Dho	Tla	295	Cve	West.	Lou	ת ו ד	300	Тчт	Ala	Tarr	Len
25	305	DCI	10th	<b>V</b> 41	* ***	310	niu	Cys	+ y +	Deu	315	Gry	- 7 -	n_a	* 7 -	320
		Ara	Gln	Val	Cvs	Ala	Leu	Glu	Lvs	Ara		Phe				520
	11011				325				_,_	330						
	(2)	INF	ORMA!	rion	FOR	SEQ	ID 1	NO:12	28:							
30																
		(i)	SE	QUEN	CE CI	HARA	CTER.	ISTIC	CS:							
			(2	A) LI	ENGTI	H: 2'	71 ar	nino	acio	a£						
						ami										
25			(1	D) T(	OPOL	OGY:	line	ear								
35		,														
		(11)	MOI	PRCOI	JE T	YPE:	pro	tein								
		(iii)	HY	POTHI	ETIC	AL: Y	YES								•	
40		/ Y	ÓB.	F (* T ) T	NT C/	arm <i>a</i> i										
40		(VI)				OURCI ISM:		i aab	- <del></del>	<u> </u>						
			\4	A) OI	KGMIV.	LOPI:	ner.	rcone	acce	с ру.	LOLI					•
	•	(ix)	. अस	ATURI	₹•						٠.					
		( 230)				KEY:	misc	e fea	ature	<b>a</b>						
45						ION :		_		-						
			``	-, -												
		(xi)	SE	QUEN	CE DI	ESCR:	IPTIC	ON: S	SEQ :	ID NO	128	3:				
	Met	Asn	Ile	Phe	Lys	Arq	Ile	Ile	Cvs	Val	Thr	Ala	Ile	Val	Leu	Gly
50	1				5				4 -	10					15	- 4
	Phe	Phe	Asn	Leu	Leu	Asp	Ala	Lys	His	His	Lys	Glu	Lys	Lys	Glu	Asp
				20		_		•	25	•			_	30		
	His	Lys	Ile 35	Thr	Arg	Glu	Leu	Lys 40	Val	Gly	Ala	Asn	Pro 45	Val	Pro	His
55		~1-	Tle	Leu	Gln	Ser	Val	Val	Asp	Asp	Leu	Lvs	Glu	Lvs	Glv	Ile

		50														
	Tare		Va 1	Tla	. Wal	Com	55 Db-	PR1	_	_		60				
	65					Ser 70					75					RΛ
5					85	Leu				90					95	-
				TOO		Leu			105					110		
	Asn	Ile	His 115	Val	Glu	Pro	Leu	Arg	Phe	Tyr	Ser	Gln	Lys 125	Ile	Thr	Asp
10	Ile	Lys 130	Asn	Leu	Lys	Lys	Gly 135	Ser		Ile	Ala		Pro	Asn	Asp	Pro
	Ala 145	Asn	Gln	Gly	Arg	Ala 150			Leu	Leu		140 Lys	Gln	Gly	Leu	
15		Leu	Lys	Asp	Pro 165	Ser	Asn	Leu	Tyr	Ala	155 Thr	Glu	Phe	qaA		
	Lys	Asn	Pro	Tyr 180		Ile	Lys	Ile			Leu	Glu	Ala		175 Leu	Leu
	Pro	Lys	Val 195		Gly	Asp	Val	Asp	185 Gly	Ala	Ile	Ile	Thr	190 Gly	Asn	Tyr
20	Ala	Leu		Ala	Lys	Leu	Thr	200 Gly	Ala	Leu	Phe	Ser	205 Glu	Asp	Lys	Asp
	Ser	210 Pro	Tyr	Ala	Asn	Leu	215 Val	Ala	Ser	Arg	Glu	220 Asp	Asn	Ala	Gln	Asp
25	225				Ala	230 Leu					235					240
23	Lys	Phe	Ile	Leu	245 Asp	Thr	Tyr	Lys	Gly	250 Ala	Ile	Ile	Pro	Ala	255 Phe	
	(0)			260			* 1		265					270		
30	(2)					SEQ										
		(1)	(P	A) LE	NGTI	IARAC I: 31	.6 an	nino		ls						
35						amin GY:					٠					
33		(ii)	MOL	ECUL	E TY	PE:	prot	ein							•	
	. (	iii)	HYP	ОТНЕ	TICA	L: Y	ES		•							
40		(vi)				URCE										
			(A	.) OR	GANI	SM:	Heli	.coba	cter	pyl	ori					
<b>1</b> 5		(ix)	(A	TURE ) NA ) LO	ME/K	EY: ON 1	misc	_fea 16	ture			٠				
		(xi)	SEQ	UENC	E DE	SCRI	PTIO	N: S	EQ I	D NO	:129	:				
50	Met (	3ln (	Glu :	Phe :	Ser 5	Leu '	Trp	Сув		Phe 10	Ile (	Glu /	Arg .		Phe 15	Leu
	Glu 1			20					Asn 25	Lys				Cys (	Gly .	
	Thr S	-	33					40					Lys :	Ser 1		
5	Tyr (	3ln /	Asp (	Glu :	Ile :	Ala 1	Lys :	Leu :	Lys (	3ly	Lys 1	Lys 2	Ala 1	Lys (	3lu :	Ile

		50					55					60				
	Tyr	Glu	Thr	Leu	Ala	Leu	Lys	Asp	Ile	Leu	Gln	Ala	Ser	Ser	Ala	Leu
	65					70					75					80
5	Met	Pro	Leu	Tyr	Glu 85	Lys	Asp	Pro	Asn	Asn 90	Gly	Tyr	Ile	Ser	Leu 95	Glu
	Ile	Asp	Pro	Phe 100	Leu	Glu	Asp	Asp	Ala 105	Ile	Lys	Ser	Ile	Asp 110	Glu	Ala
	Lys	Arg	Leu 115	Phe	Lys	Thr	Leu	Asn 120	Arg	Pro	Asn	Val	Met 125	Ile	Lys	Val
10	Pro	Ala 130	Ser	Glu	Ser	Ala	Phe 135	Glu	Val	Ile	Ser	Ala 140	Leu	Ala	Gln	Ala
	Ser	Ile	Pro	Ile	Asn	Val		Leu	Val	Phe	Ser		Lys	Ile	Ala	Gly
	145					150		-			155					160
	Glu	Ile	Ala	Gln	Ile	Leu	Ala	Lys	Glu	Ala	Arg	Lys	Arg	Ala	Val	Ile
15					165			-		170	_	_			175	
	Ser	Val	Phe	Val 180	Ser	Arg	Phe	Asp	Lys 185	Glu	Ile	Asp	Pro	Leu 190	Val	Pro
	Gln	Asn	Leu 195	Gln	Ala	Gln	Ser	Gly 200	Ile	Met	Asn	Ala	Thr 205	Glu	Cys	Tyr
20	Tyr	Gln 210	Ile	Asn	Gln	His	Ala 215	Asn	Lys	Leu	Ile	Ser 220	Thr	Leu	Phe	Ala
٠	Ser 225	Thr	Gly	Val	ГÀЗ	Ser 230	Asn	Ser	Leu	Ala	Lys 235	Asp	Tyr	Tyr	Ile	Lys 240
25	Ala	Leu	Cys	Phe	Lys 245	Asn	Ser	Ile	Asn	Thr 250	Ala	Pro	Leu	Asp	Ala 255	Leu
	Asn	Ala	Tyr	Leu 260	Leu	Asp	Pro	Asn	Thr 265	Glu	Cys	Gln	Thr	Pro 270	Leu	Lys
	Ile	Thr	Glu 275	Ile	Glu	Ala	Phe	Lys 280	Lys	Glu	Leu	Lys	Thr 285	His	Asn	Ile
30	Asp	Leu 290	Glu	Asn	Thr	Ala	Gln 295	Lys	Leu	Leu	Lys	Glu 300	Gly	Leu	Ile	Ala
	Phe	Lys	Gln	Ser	Phe	Glu	Lys	Leu	Leu	Ser	Ser	Phe				
	305					310					315					
35	(2)	INF	ORMA!	rion	FOR	SEQ	ID 1	10:13	30:							
		(i)	(2	A) LI	engti	HARAC	50 ar	nino		is						
40				-		amiı DGY:							٠			
		(ii)	MOI	LECUI	LE T	YPE:	prot	tein								

- (iii) HYPOTHETICAL: YES

- (ix) FEATURE:

  (A) NAME/KEY: misc\_feature
  (B) LOCATION 1...260
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:
- 55 Met Lys Thr Asn Gly His Phe Lys Asp Phe Ala Trp Lys Lys Cys Phe

	1				5					10					15	
	Leu	Gly	Ala	Ser	Val	Val	Ala	Leu	Leu		Glv	Cvs	Ser	Pro	Hiq	Ile
			•	20					25		1	-7-		30	*****	
	Ile	Glu	Thr	Asn	Glu	Val	Ala	Leu	Lys	Leu	Asn	Tvr	His	Pro	Ala	Ser
:5			35					40					45			
	Glu	Lys	Val	Gln	Ala	Leu	Asp	Glu	Lys	Ile	Leu	Leu	Leu	Arg	Pro	Ala
		50					55	*				60				
	Phe	Gln	Tyr	Ser	Asp	Asn	Ile	Ala	Lys	Glu	Tyr	Glu	Asn	Lys	Phe	Lys
10	65					70					75					80
10	Asn	Gln	Thr	Thr	Leu	Lys	Val	Glu	Glu	Ile	Leu	Gln	Asn	Gln	Gly	Tyr
	_			_	85					90					95	
	Lys	Val	IIe	Asn	Val	Asp	Ser	Ser		Lys	Asp	Asp	Phe	Ser	Phe	Ala
	<b>~</b> 1~	7	T	100	<b>63</b>	_	_		105					110		
15	GIII	Lys	ьув 115	GIU	GTA	Tyr	Leu		Val	Ala	Met	Asn	Gly	Glù	Ile	Val
13	Ton	λ ~~		7	Dage	T	•	120					125			
	пеп	130	PIO	Asp	ė.	гуѕ		Thr	Ile	Gin	Lys		Ser	Glu	Pro	Gly
	T.e.ii		Dhe	Ser	Thr	G1 vz	135	<b>3</b>	T	<b>N</b> = 4-	~7	140		_		
	145		4 110	Der	1111	150	Leu	Asp	ьys	Met		Arg	Val	Leu	Ile	
20		Glv	Phe	Val	Lvs		Thr	Ile	T.e.u	<i>c</i> 1	155	<b>M</b> -+		<b>~</b> 3		160
					165			116	шец	170	PIQ	Mec	ser	GIA		ser
	Leu	Asp	Ser	Phe	Thr	Met	asa	Leu	Ser		T.e.v	λen	T10	GI n	175	T
		-		180					185			nsp	116	190	GIU	гуя
	Phe	Leu	Lys	Thr	Thr	His	Ser	Ser		Ser	Glv	Glv	Leu	Val	Ser	Thr
25		-	195					200					205		+	
	Met	Val	Lys	Gly	Thr	Asp	Asn	Ser	Asn	Asp	Ala	Ile	Lvs	Ser	Ala	Leu
		210					215					220				
	Asn	Lys	Ile	Phe	Ala	Ser	Ile	Met	Gln	Glu	Mèt	Asp	Lys	Lys	Leu	Thr
20	225					230					235					240
30	Gln	Arg	Asn	Leu	Glu	Ser	Tyr	Gln	Lys	Asp	Ala	Lys	Glu	Leu	Lys	Asn
					245					250					255	
	гÃг	Arg	Asn	_												
				260												•
35	(2)	TNEC	יי גיאסי	TON	EOD	CEO	TD 1	TO:13	-							
	(2)	1111-0	, rains t	1014	FOR	SEQ	י עד	10:13	Τ:			*				
		(i)	SEC	TENC	E CH	APAC	ו סשייי	STIC	· c .							
		,-,						mino		de						
			(B	) TY	PE:	amin	o ac		acı	.us	•					
40						GY:								,		
ſ																
		(ii)	MOL	ECUL	E TY	PE:	prot	ein								

- (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...1382
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:
- 55 Leu Asn Phe Asn Asn Leu Thr Ala Asn Gly Ala Leu Asn Phe Asn Gly

	1				5					10					15	•
		Ala	Pro	Ser 20	_	Thr	Lys	Ala			Asn	Val	Ser	Gly 30		Phe
5			35			Gly		40				_	45			
		50				Ser	55					60				
	65					Ser 70					75					80
10					85	Gln				90		_			95	
٠				100		Ile			105					110	•	
15			115			Gly Thr		120					125			
		130				Gln	135			٠.		140			_	
20	145					150 Thr					155		_	_	_	160
					165	Ser				170					175	
				180		Leu			185				_	190		
25	Ser	Ser	195 Glu	Asn	Leu	Lys	Thr	200 Leu	Leu	Gly	Ile	Leu	205 Ser	Gln	Asn	Ser
		210 Thr	Leu	Lys	Glu	Met	215 Ile	Glu	Ser	Asn		220 Leu	Asp	Asn	Ile	
30	225 Asn	Ile	Asn			230 Leu	Gln	Leu	Leu		235 Lys	Ile	Lys	Ile		240 Gln
	Ala	Gln	Lys		245 Ala	Leu	Leu	Glu	Thr 265	250 Ile	Asn	His	Leu		255 Asp	Asn
35	Ile	Asn	Gln 275		Phe	Asn	Asn	Gly 280		Leu	Val	Ile	Gly 285	270 Ala	Thr	Gln
	Asp	Asn 290		Thr	Asn	Ser	Thr 295		Ser	Ile	Trp	Phe	Gly	Gly	Asn	Gly
	Tyr 305	Ser	Ser	Pro	Суѕ	Ala 310	Leu	Asp	Ser	Ala	Thr 315			Ser	Phe	Arg 320
40					325	Gln				330	•				335	
				340		Phe			345					350		
45	•		355			Ala		360					365			
. •		370				Asn	375					38.0				
50	385					Ile 390					395			_		400
50					405	Gly Gln				410					415	
				420		Ser			425					430		
55			435				_,,	440					445		-wp	Jiu

	Thi	Lei 450	ı Gl	y Glr	n Lei	u Ile	Gl <sub>3</sub>	/ Glr	Ası	a Asr	ı Leı	1 Asj 460		) Le	ı Le	u Asn
	Asr 465	ı Se:	r Gly	y Val	l Met	470	ı Glu	ı Ile	e Glr	a Asr	1 Ile 475	: Ile	Se:	Gli	ı Ly	s Leu
5	Sei	r Ile	Phe	e Gly	7 Ası 485	n Phe		Thr	Pro	Ser 490	: Ile	· Ile	e Glu	ı Ası		480 r Leu
	Ala	Lys	Glr	n Ser 500	Let	ı Lys	S Ser	Met	Lev 505	a Asp	Asp	Lys	Gly			ı Asn
10	Phe	: Ile	Gly 515	/ Gly	у Туз	: Ile	Asp	Ala 520	Ser		Leu	Ser	Ser 525		Let	ı Gly
	Val	. Ile	e Let	ı Lys	s Asp	o Ile	Thr. 535	Asn		Pro	Thr	Ser 540	Lev	Gln	Lys	Asp
	Ile 545	Gly	v Val	l Val	Ala	Asn 550	Asp		Leu	Asn		Phe	Leu	Gly	Glr	a Asp
15			Lys	Lys	Leu	Glu		Gln	Gly	Leu	555 Val	Ser	Asn	Ile	: Ile	560. Asn
				Ser	Gln	•			Ser	570 Gly					575	
				. 560	,				585					590		Asp
20			222	•				600					605			
		OTO	ı				615					620				Lys
	Gly 625	Tyr	Phe	: Asn	Phe	Leu 630	Ser	Asn	Gly	Tyr		Phe	Val	Asn	Asn	Ser
25	Ser	Phe	Ser	Asn	Ala 645	Thr		Gly	Ser	Leu 650	635 Asn	Phe	Val	Ala		640 Lys
	Ser	Ile	Ile	Phe 660	Asn	Gly	Asp	Asn	Thr	Ile	Asp	Phe	Ser	Lys	655 Tyr	Gln
30	Gly	Ala	Leu 675	Ile		Ala	Ser	Asn	665 Gly	Val	Ser	Asn		670 Asn	Ile	Thr
,	Thr	Leu 690			Thr	Asn	Gly 695	680 Leu	Ser	Leu	Asn		685 Gly	Leu	Asn	Asn
	Val		Val	Gln	Lys	Gly	Glu	Ile	Cys	Ile	Asn	700 Leu	Ala	Asn	Суз	Pro
35	,05					710 Ser					715					720
					725	His				730					725	
				/40					745					750		
40			133			Ile		760					765			
		,,,				Leu	775					780				
	љец 785	Inr	IIe	Thr	Asn.	Ala 790	Phe	Asn	Asn	Ala	Ser 795		Ser	Thr	Ala	
45				•	805	Thr				810	Ala	Thr			915	
				02U		Val			825	Phe				830	Asp	
50			033			His		840					945	Asn		
		030				Met	855					960	Ile			
56	003					Val 870					Leu 875	Ile				000
55	А1а	ITE	Tyr	Tyr	Gly	Tyr	Asn	Asn	Gln	Ile	Thr	Gly	Gly	Ser	Ser	Leu

					885					890			1		895	
٠.			Tyr	900					905					910	_	
5			Met 915					920				_	925	,		
	Val	930					935					940		•		
	Tyr 945	Ile	Tyr	Thr	Ser	Ile 950	Leu	Tyr	Asn	Lys	Val 955	Lys	Ile	Ala	Val	Ser 960
10		_	Pro		965					970			_		975	
	Ala			980					985					990		_
15			Gln 995					1000	0				100	5	_	-
		1010					101	5				1026	0			
	1025	5	Thr			1030	)				103	5				104
20			Asn		104	5				105	0				105	5
			Gln	1060	)				1069	5				1070	)	
25	Phe	Ala	Arg 107!		Asp	Phe	Leu	Glu 108		Leu	Glu	Ala	Leu 1089		Asn	Lys
	Arg	Phe 1090	Ala )	Asp	Ala	Ile	Pro 109		Ala	Met	Asp	Val		Leu	Lys	Tyr
	Ser 1109		Arg	Asn	Arg	Val 1110		Asn	Asn	Val	Trp 1119		Thr	Gly	Val	Gly 1120
30	Gly	Ala	Ser	Phe	Ile 112		Gly	Gly	Thr	Gly 113		Leu	Tyr	Gly	Ile 1135	
			Tyr	1140	)				1145	5				1150	)	
35			Gly 115	5				1160	)				1169	5	-	
		1170					1175	5				1180	)			
	1185	5	Thr			1190	)				1199	5				1200
40	Ile	Asn	Ser	Tyr	Asp 120		Leu	Leu	Ser	Ile 121		Asn	Gln	Ser	Tyr 1215	
			Thr	1220	)				1225	5		-	-	1230	)	
45	Met	Phe	Lys 1239		Lys	Ser	Val	Ile 1240		Lys	Pro	Gln	Val 1245		Leu	Ser
		1250	•				1255	5				1260	)			
	1265	5	Asn			1270	)				1275	5				1280
50			Ile		1285	5				1290	)				1295	5 `
			Tyr	1300	)				1305	;				1310	1	
55	Ser	Met	Gly 1315	Asp		Met		Arg 1320		Ile	Gly	Asn	Asn 1325		Leu	Ser

```
Tyr Arg Asp Gly Gly Arg Tyr Asn Thr Phe Ala Ser Ile Ile Thr Gly
                        1335
                                            1340
Gly Glu Ile Arg Leu Phe Lys Thr Phe Tyr Val Asn Ala Gly Ile Gly
                    1350
                                       1355
Ala Arg Phe Gly Leu Asp Tyr Lys Asp Ile Asn Ile Thr Gly Asn Ile
                                    1370
Gly Met Arg Tyr Ala Phe
            1380
(2) INFORMATION FOR SEQ ID NO:132:
```

- 10
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 262 amino acids
    - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

- 20
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

55

- 25 (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...262
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:
- 30 Met Lys Lys Ile Gly Leu Ser Leu Cys Leu Val Leu Ser Leu Gly Phe 10 Leu Lys Ala His Glu Val Ser Ala Glu Glu Ile Ala Asp Ile Phe Tyr 25 Lys Leu Asn Ala Lys Glu Pro Lys Met Lys Ile Asn His Thr Lys Gly 35 40 Phe Cys Ala Lys Gly Val Phe Leu Pro Asn Pro Gln Ala Arg Glu Asp Leu Glu Val Pro Leu Leu Asn Glu Lys Glu Ile Pro Ala Ser Val Arg 70 40 Tyr Ser Leu Gly Gly Val Ala Met Asp Asp Lys Ser Lys Val Arg Gly 90 Met Ala Leu Lys Leu Glu Asn Gln Asn Ala Ser Trp Thr Met Val Met 100 105 Leu Asn Thr Glu Ile Asn Phe Ala Lys Asn Pro Glu Glu Phe Ala Gln 45 120 Phe Phe Glu Met Arg Leu Pro Lys Asn Gly Lys Val Asp Glu Ala Arg 135 140 Ile Lys Lys Leu Tyr Glu Glu Val Pro Ser Tyr Arg Asn Phe Ala Ala 150 155 Tyr Met Lys Thr Ile Gly Ile Ser Ser Ser Val Ala Asn Thr Pro Tyr 50 165 170 Tyr Ser Val His Ala Phe Lys Phe Lys Asp Lys Lys Glu Lys Leu Leu

185 Pro Ala Arg Trp Lys Phe Val Pro Lys Glu Gly Val Lys Tyr Leu Asn

WO 98/18323 PCT/US97/19575

Pro Gln Glu Leu Lys Gln Lys Asp Ser Asn Tyr Leu Leu Ser Ser Phe 215 Gln Gln His Leu Lys Asn Lys Pro Ile Glu Tyr Gln Met Tyr Leu Val 230 235 Phe Ala Asn Gln Asn Asp Ala Thr Asn Asp Thr Thr Ala Leu Trp Lys 250 Gly Ser Ile Arg Asn Tyr 260

- 10 (2) INFORMATION FOR SEQ ID NO:133:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 246 amino acids
    - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:
- 25 -(A) NAME/KEY: misc feature
  - (B) LOCATION 1...246
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:
- 30 Met Lys Gln Phe Lys Lys Lys Pro Lys Lys Ile Lys Arg Ser His Gln Asn Gln Lys Thr Ile Leu Lys Arg Pro Leu Trp Leu Met Pro Leu Leu Ile Gly Gly Phe Ala Ser Gly Val Tyr Ala Asp Gly Thr Asp Ile Leu 35 Gly Leu Ser Trp Gly Glu Lys Ser Gln Lys Val Cys Val His Arg Pro Trp Tyr Ala Ile Trp Ser Cys Asp Lys Trp Glu Glu Lys Thr Gln Gln 75 40 Phe Thr Gly Asn Gln Leu Ile Thr Lys Thr Trp Ala Gly Gly Asn Ala 85 90
- Ala Asn Tyr Tyr His Ser Gln Asn Asn Gln Asp Ile Thr Ala Asn Leu 105
- Lys Asn Asp Asn Gly Thr Tyr Phe Leu Ser Gly Leu Tyr Asn Tyr Thr 45 120 .
  - Gly Gly Glu Tyr Asn Gly Gly Asn Leu Asp Ile Glu Leu Gly Ser Asn 135
  - Ala Thr Phe Asn Leu Gly Ala Ser Ser Gly Asn Ser Phe Thr Ser Trp 150 155
- 50 Tyr Pro Asn Gly His Thr Asp Val Thr Phe Ser Ala Gly Thr Ile Asn 170
  - Val Asn Asn Ser Val Glu Val Gly Asn Arg Val Gly Ser Gly Ala Gly 185 Thr His Thr Gly Thr Ala Thr Leu Asn Leu Asn Ala Asn Lys Val Thr
- 55 195 200

Ile Asn Ser Asn Ile Ser Ala Tyr Lys Thr Ser Gln Val Asn Val Gly
210
215
220
Asn Ala Asn Ser Val Ile Thr Ile Asn Ser Val Ser Leu Asn Gly Glu
225
230
235
240

Tyr Leu Gln Phe Phe Ser
245

(2) INFORMATION FOR SEQ ID NO:134:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 245 amino acids
(B) Type: amino acid

15 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

(D) TOPOLOGY: linear

(ix) FEATURE:

(A) NAME/KEY: misc\_feature

(B) LOCATION 1...245

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

Met Ile Lys Lys Thr Leu Ala Ser Val Leu Leu Gly Leu Ser Leu Met Ser Val Leu Asn Ala Lys Glu Cys Val Ser Pro Ile Thr Arg Ser Val 20 Lys Tyr His Gln Gln Ser Ala Glu Ile Arg Ala Leu Gln Leu Gln Ser 40 Tyr Lys Met Ala Lys Met Ala Leu Asp Asn Asn Leu Lys Leu Val Lys 35 Asp Lys Lys Pro Ala Val Ile Leu Asp Leu Asp Glu Thr Val Leu Asn 70 Thr Phe Asp Tyr Ala Gly Tyr Leu Val Lys Asn Cys Ile Lys Tyr Thr 40 Pro Glu Thr Trp Asp Lys Phe Glu Lys Glu Gly Ser Leu Thr Leu Ile 100 105 Pro Gly Ala Leu Asp Phe Leu Glu Tyr Ala Asn Ser Lys Gly Val Lys 120 Ile Phe Tyr Ile Ser Asn Arg Thr Gln Lys Asn Lys Ala Phe Thr Leu 45 135 Lys Thr Leu Lys Ser Phe Lys Leu Pro Gln Val Ser Glu Glu Ser Val 150 155 Leu Leu Lys Glu Lys Gly Lys Pro Lys Ala Val Arg Arg Glu Leu Val 165 170 Ala Lys Asp Tyr Ala Ile Val Leu Gln Val Gly Asp Thr Leu His Asp 180 185 Phe Asp Ala Ile Phe Ala Lys Asp Ala Lys Asn Ser Gln Glu Gln Gln 200 Ala Lys Val Leu Gln Asn Ala Gln Lys Phe Gly Thr Glu Trp Ile Ile 55 215

WO 98/18323 PCT/US97/19575

- 215 -

5

- (2) INFORMATION FOR SEQ ID NO:135:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 288 amino acids
- 10 (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
- 15 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
- 20 (ix) FEATURE:
  - (A) NAME/KEY: misc feature
  - (B) LOCATION 1...288
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

Leu Trp Cys Leu Lys Thr Pro Ile Ile Gly His Gly Met Lys Lys Lys 1 5 10 15

Ala Lys Val Phe Trp Cys Cys Phe Lys Met Ile Arg Trp Leu Tyr Leu 20 25 30

30 Ala Val Phe Phe Leu Leu Ser Val Ser Asp Ala Lys Glu Ile Ala Met

35 40 45
Cln Arg Phe Agn Lye Cln Agn Hig Lye Tlo Pho Cly Tlo Loy Ala Agn

Gln Arg Phe Asp Lys Gln Asn His Lys Ile Phe Glu Ile Leu Ala Asp 50 55 60

Lys Val Ser Ala Lys Asp Asn Val Ile Thr Ala Ser Gly Asn Ala Ile 35 65 70 75 80

Leu Leu Asn Tyr Asp Val Tyr Ile Leu Ala Asp Lys Val Arg Tyr Asp 85 90 95

Thr Lys Thr Lys Glu Ala Leu Leu Glu Gly Asn Ile Lys Val Tyr Arg
100 105 110

40 Gly Glu Gly Leu Leu Val Lys Thr Asp Tyr Val Lys Leu Ser Leu Asn 115 120 125

Glu Lys Tyr Glu Ile Ile Phe Pro Phe Tyr Val Gln Asp Ser Val Ser 130 135 140

Gly Ile Trp Val Ser Ala Asp Ile Ala Ser Gly Lys Asp Gln Lys Tyr 45 145 150 155 160

145 150 155 160
Lys Ile Lys Asn Met Ser Ala Ser Gly Cys Ser Ile Asp Asn Pro Ile

Trp His Val Asn Ala Thr Ser Gly Ser Phe Asn Met Gln Lys Ser His
180 185 190

50 Leu Ser Met Trp Asn Pro Lys Ile Tyr Val Gly Asp Ile Pro Val Leu 195 200 205

Tyr Leu Pro Tyr Ile Phe Met Ser Thr Ser Asn Lys Arg Thr Thr Gly 210 215 220

Phe Leu Tyr Pro Glu Phe Gly Thr Ser Asn Leu Asp Gly Phe Ile Tyr 225 230 235 240

Leu Gln Pro Phe Tyr Leu Ala Pro Lys Asn Ser Trp Asp Met Thr Phe

245 250 255

Thr Pro Gln Ile Arg Tyr Lys Arg Gly Phe Gly Leu Asn Phe Glu Ala

260 265 270

Arg Tyr Ile Asn Ser Lys Thr Gln Val Phe Ile Gln Cys Ala Leu Phe

275 280 285

- (2) INFORMATION FOR SEQ ID NO:136:
- 10 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 128 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 15 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc\_feature
    - (B) LOCATION 1...128

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:
- Leu Met Phe Lys Lys Met Cys Leu Ser Leu Leu Met Ile Ser Gly Val
- Cys Val Gly Ala Lys Asp Leu Asp Phe Lys Leu Asp Tyr Arg Ala Thr
  - Gly Gly Lys Phe Met Gly Lys Met Thr Asp Ser Ser Leu Leu Ser Ile 35 40 45
- Thr Ser Met Asn Asp Glu Pro Val Val Ile Lys Asn Leu Ile Val Asn So 50 55
  - Arg Gly Asn Ser Cys Glu Ala Thr Lys Lys Val Glu Pro Lys Phe Gly 65 70 75 80
  - Asp Lys Phe Lys Lys Glu Lys Leu Phe Asp His Glu Leu Lys Tyr Ser
- 40 Gln Gln Ile Phe Tyr Arg Leu Asp Cys Lys Pro Asn Gln Leu Leu Glu
  100 105 110
  - Val Lys Ile Ile Thr Asp Lys Gly Glu Tyr Tyr His Lys Phe Ser Lys
    115
    120
    125
- 45 (2) INFORMATION FOR SEQ ID NO:137:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 169 amino acids
    - (B) TYPE: amino acid
- 50 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:
- (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...169
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:
- 10 Met Gln Ala Leu Lys Ser Leu Leu Glu Val Ile Thr Lys Leu Gln Asn
  1 5 10 15

Leu Gly Gly Tyr Leu Met His Ile Ala Ile Phe Ile Ile Phe Ile Trp
20 25 30

Ile Gly Gly Leu Lys Phe Val Pro Tyr Glu Ala Glu Gly Ile Ala Pro
15 40 45

Phe Val Ala Asn Ser Pro Phe Phe Ser Phe Met Tyr Lys Phe Glu Lys 50 55 60

Pro Ala Tyr Lys Gln His Lys Met Ser Glu Ser Gln Ser Met Gln Glu 65 70 75 80

20 Glu Met Gln Asp Asn Pro Lys Ile Val Glu Asn Lys Glu Trp His Lys 85 90 95

Glu Asn Arg Thr Tyr Leu Val Ala Glu Gly Leu Gly Ile Thr Ile Met 100 105 110

Ile Leu Gly Ile Leu Val Leu Leu Gly Leu Trp Met Pro Leu Met Gly
25 115 120 125

Val Val Gly Gly Leu Leu Val Ala Gly Met Thr Ile Thr Thr Leu Phe 130 135 140

Phe Phe Ile His Asn Ala Arg Ser Val Cys Gln Ser Ala Phe Pro Met 145 150 155 160

30 Ala Phe Trp Gly Trp Lys Ala Ser Gly 165

- (2) INFORMATION FOR SEQ ID NO:138:
- 35 (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 487 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- 40 (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
- 45 (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

50

- (A) NAME/KEY: misc feature
- (B) LOCATION 1...487
- (xi) SEQUENCE DESCRIPTION: SEO ID NO:138:

Met Ile Glu Trp Met Gln Asn His Arg Lys Tyr Leu Val Val Thr Ile

1 5 10 15

55 Trp Ile Ser Thr Ile Ala Phe Ile Ala Ala Gly Met Ile Gly Trp Gly

				20					2.5							
	Gln	Tyr	Ser		Ser	Leu	Asp	Ser	25 Asn	Ser	. Ala	בות	Taro	30 [eV	<i>(</i> 111)	Gln
			35					40					45			
5		50	-				55					60				Lys
	65					70					75					Asp 80
					85					90					95	Ile
10				100					105					110		Ala
			115					120					125			Gln
15		130					135					140				Gln
	145					150					155					Leu 160
20					165					170					175	
20				180					185		Leu			190		
			195					200					205			Glu
25		210			*		215					220				Pro
٠	225					230					235					Lys 240
30					245					250	His				255	
				260					265		Phe Ala			270		
			275					280			Ala		285			
35		290					295				Thr	300				
	305					310					315 Leu					320
40					325					330	Ser				335	
				340					345		Leu			350		
45		Glu	355					360			Leu		365		•	
45	Lys	370				Lys	375					380				
•	385				Glu	390				Glu	395 Ser					400
50	Thr	Leu	Phe	Asn	405 Arg	Gln	Glu	Lys		410 Gly	Phe	Val	Thr	Ile	415 Gly	Asn
•	Lys	Val	Val 435	420 Leu	Tyr	Gln	Ile		425 Glu	Gln	Asn	Phe		430 His	Pro	Phe
55	Ser	Ala 450		Glu	Asn		Tyr 455	440 Met	Gln	Arg	Leu		445 Asn	Asn	Thr	Lys
							* 7 2					460				

Thr Asp Phe Phe Asp Lys Ala Leu Ile Glu Glu Leu Lys Lys Arg Tyr 465 470 475 480

Lys Ile Val Lys Tyr Ile Gln
485

5

25

- (2) INFORMATION FOR SEQ ID NO:139:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 142 amino acids
- 10 (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
- 15 (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
- 20 (ix) FEATURE:
  - (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...142
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:
  - .

Met Lys Thr Asn Phe Tyr Lys Ile Lys Leu Leu Phe Ala Trp Cys Leu 1 5 10 15

Ile Ile Gly Met Phe Asn Ala Pro Leu Asn Ala Asp Gln Asn Thr Asp 20 25 30

30 Ile Lys Asp Ile Ser Pro Glu Asp Met Ala Leu Asn Ser Val Gly Leu 35 40 45

Val Ser Arg Asp Gln Leu Lys Ile Glu Ile Pro Lys Glu Thr Leu Glu
50 55 60

Gln Lys Val Ala Ile Leu Asn Asp Tyr Asn Asp Lys Asn Val Asn Ile 35 65 70 75 80

Lys Phe Asp Asp Ile Ser Leu Gly Ser Phe Gln Pro Asn Asp Asn Leu 85 90 95

Gly Ile Asn Ala Met Trp Gly Ile Gln Asn Leu Leu Met Ser Gln Met
100 105 110

40 Met Ser Asn Tyr Gly Pro Asn Asn Ser Phe Met Tyr Gly Tyr Ala Pro
115 120 125

Thr Tyr Ser Asp Ser Ser Phe Leu Pro Pro Ile Leu Gly Tyr 130 135 140

- 45 (2) INFORMATION FOR SEQ ID NO:140:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 208 amino acids
    - (B) TYPE: amino acid
- 50 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

```
(vi) ORIGINAL SOURCE:
     (A) ORGANISM: Helicobacter pylori
```

#### (ix) FEATURE:

5 (A) NAME/KEY: misc\_feature

(B) LOCATION 1...208

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

- Leu Ile Asn Asn Asn Asn Asn Lys Lys Leu Arg Gly Phe Phe Leu 10 Lys Val Leu Leu Ser Leu Val Val Phe Ser Ser Tyr Gly Ser Ala Asn Asp Asp Lys Glu Ala Lys Lys Glu Ala Leu Glu Lys Glu Lys Asn Thr 15 Pro Asn Gly Leu Val Tyr Thr Asn Leu Asp Phe Asp Ser Phe Lys Ala Thr Ile Lys Asn Leu Lys Asp Lys Lys Val Thr Phe Lys Glu Val Asn 75 Pro Asp Ile Ile Lys Asp Glu Val Phe Asp Phe Val Ile Val Asn Arg 90 Val Leu Lys Lys Ile Lys Asp Leu Lys His Tyr Asp Pro Val Ile Glu 105 Lys Ile Phe Asp Glu Lys Gly Lys Glu Met Gly Leu Asn Val Glu Leu 25 120 Gln Ile Asn Pro Glu Val Lys Asp Phe Phe Thr Phe Lys Ser Ile Ser 135 Thr Thr Asn Lys Gln Arg Cys Phe Leu Ser Leu His Gly Glu Thr Arg 150 155 Glu Ile Leu Cys Asp Asp Lys Leu Tyr Asn Val Leu Leu Ala Val Phe 30 170 Asn Ser Tyr Asp Pro Asn Asp Leu Leu Lys His Ile Ser Thr Ile Glu 185 Ser Leu Lys Lys Ile Phe Tyr Thr Ile Thr Cys Glu Ala Val Tyr Leu 35 200
  - (2) INFORMATION FOR SEQ ID NO:141:
    - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 245 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

50
(ix) FEATURE:

40

45

(A) NAME/KEY: misc\_feature

(B) LOCATION 1...245

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Met Ala Gly Thr Gln Ala Ile Tyr Glu Ser Ser Ala Gly Phe Leu Ser Gln Val Ser Ser Ile Ile Ser Ser Thr Ser Gly Val Ala Gly Pro Phe Ala Gly Ile Val Ala Gly Ala Met Thr Ala Ala Ile Ile Pro Ile 40 Val Val Gly Phe Thr Asn Pro Gln Met Thr Ala Ile Met Thr Gln Tyr 55 10 Asn Gln Ser Ile Ala Glu Ala Val Ser Val Pro Met Lys Ala Ala Asn 70 Gln Gln Tyr Asn Gln Leu Tyr Gln Gly Phe Asn Asp Gln Ser Met Ala 90 Val Gly Asn Asn Ile Leu Asn Ile Ser Lys Leu Thr Gly Glu Phe Asn 15 105 Ala Gln Gly Asn Thr Gln Ser Ala Gln Ile Ser Ala Val Asn Ser Gln 120 Ile Ala Ser Ile Leu Ala Ser Asn Thr Thr Pro Lys Asn Pro Ser Ala 135 140 20 Ile Glu Ala Tyr Ala Thr Asn Gln Ile Ala Val Pro Ser Val Pro Thr 150 155 Thr Val Glu Met Met Ser Gly Ile Leu Gly Asn Ile Thr Ser Ala Ala 165 . . 170 Pro Lys Tyr Ala Leu Ala Leu Gln Glu Gln Leu Arg Ser Gln Ala Ser 25 180 185 Asn Ser Ser Met Asn Asp Thr Ala Asp Ser Leu Asp Ser Cys Thr Ala 200 Leu Gly Ala Leu Val Gly Ser Ser Lys Val Phe Phe Ser Cys Met Gln 215 220 30 Ile Ser Met Thr Pro Met Ser Val Ser Met Pro Thr Val Met Pro Asn 235 Thr Ser Gly Cys His (2) INFORMATION FOR SEQ ID NO:142: 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 367 amino acids

- - (B) TYPE: amino acid
- 40 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES
  - (vi) ORIGINAL SOURCE:
    - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:

45

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...367
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:
- 55 Met Ile Lys Ser Val Glu Ile Glu Asn Tyr Lys Asn Phe Glu His Leu

	1				5					10					15	
				20					25	Phe				30	Asn	Asp
5			35					40					45			Leu
		50					55					60				Val
10	65					70					75					Lys 80
10					85					90					95	Thr
				100					105					110		Gln
15	-		112					120					125			Met
		T20				Thr	135					140				
20	145					150					155					Arg 160
20					165					170					175	Thr
				180		Met			185					190		
25			195			Glu		200					205			
		210				Gln	215					220				
30	225					Val 230					235					240
-					245	Lys				250					255	
				260		Met			265					270		
35			2/5			Glu Ala		280					285			
		290				Thr	295					300				
40	305 Asn					310					315					320
					325	Glu				330					22E	
				340		Ala			345					350		Tyr
15			355		-,, -			360	ALY.	дтÅ	MEL	GIU	365	Arg	стА	

# (2) INFORMATION FOR SEQ ID NO:143:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 409 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

### (iii) HYPOTHETICAL: YES

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Helicobacter pylori

5

### (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- (B) LOCATION 1...409
- 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

	Met 1	Ser	Leu	Ile	Arg 5	Val	Asn	Gly	Glu	Ala 10	Phe	Lys	Leu	Ser	Leu 15	Glu
15				20					25					30		Leu
			35					40					45	Ala	_	
20		50					55					60		Arg		
20	65					70					75			Glu		80
					85					90				Tyr	95	
25				100			*		105					Gly 110		
			115		•			120					125	Ser		-
20		130					135					140		Glu		
30	145					150					155			Cys		160
					165					170				Glu	175	
<b>35</b> .				180					185					Ser 190		
			195					200					205	Asp		
40		210					215					220		Ile		_
<b>7</b> 0	225					230					235			Lys		240
					245					250				Met	255	
45				260			•		265					Gly 270		
			275					280					285	Gly		
50		290					295					300		Lys		
50	305		•			310					315			Lys		320
					325					330				Gln	335	•
55	сту	rue	GIU	340	Leu	GIU	мес	GTA	345	ınr	тте	Phe	ser	Glu 350	īīe	Pro

Lys Ile Thr Pro Tyr Lys Pro Ala Ile Leu Glu Asn Leu Ser Gln Leu 360 Leu Gly Leu Glu Lys Ser Gln Ile Ser Leu Lys Ala Thr Thr Met Glu 375 380 Lys Met Gly Phe Ile Gly Lys Gln Glu Gly Leu Leu Val Gln Ala His 390 395 Val Ser Met Arg Tyr Lys Gln Lys Leu

- (2) INFORMATION FOR SEQ ID NO:144: 10
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 270 amino acids
    - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (iii) HYPOTHETICAL: YES

20

25

55

- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
- (ix) FEATURE:
- (A) NAME/KEY: misc\_feature
  - (B) LOCATION 1...270
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:
- 30 Met Lys Lys Phe Val Ala Leu Gly Leu Leu Ser Ala Val Leu Ser Ser Ser Leu Leu Ala Glu Gly Asp Gly Val Tyr Ile Gly Thr Asn Tyr Gln Leu Gly Gln Ala Arg Leu Asn Ser Asn Ile Tyr Asn Thr Gly Asp Cys 35 40 Thr Gly Ser Val Val Gly Cys Pro Pro Gly Leu Thr Ala Asn Lys His 55 Asn Pro Gly Gly Thr Asn Ile Asn Trp His Ser Lys Tyr Ala Asn Gly . 75 Ala Leu Asn Gly Phe Gly Leu Asn Val Gly Tyr Lys Lys Phe Phe Gln 40 Phe Lys Ser Leu Asp Met Thr Ser Lys Trp Phe Gly Phe Arg Val Tyr 105 Gly Leu Phe Asp Tyr Gly His Ala Asp Leu Gly Lys Gln Val Tyr Ala 45 120 Pro Asn Lys Ile Gln Leu Asp Met Val Ser Trp Gly Val Gly Ser Asp 135 140 Leu Leu Ala Asp Ile Ile Asp Lys Asp Asn Ala Ser Phe Gly Ile Phe 150 155 Gly Gly Val Ala Ile Gly Gly Asn Thr Trp Lys Ser Ser Ala Ala Asn 50 170 Tyr Trp Lys Glu Gln Ile Ile Glu Ala Lys Gly Pro Asp Val Cys Thr 185 Pro Thr Tyr Cys Asn Pro Asn Ala Pro Tyr Ser Thr Asn Thr Ser Thr

WO 98/18323 PCT/US97/19575

- 225 -Val Ala Phe Gln Val Trp Leu Asn Phe Gly Val Arg Ala Asn Ile Tyr 215 Lys His Asn Gly Val Glu Phe Gly Val Arg Val Pro Leu Leu Ile Asn 235 Lys Phe Leu Ser Ala Gly Pro Asn Ala Thr Asn Leu Tyr Tyr His Leu 250 Lys Arg Asp Tyr Ser Leu Tyr Leu Gly Tyr Asn Tyr Thr Phe 10 (2) INFORMATION FOR SEQ ID NO:145: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 438 amino acids (B) TYPE: amino acid 15 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: YES 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori (ix) FEATURE: 25 (A) NAME/KEY: misc feature (B) LOCATION 1...438 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:145: Met Ala Tyr Lys Pro Asn Lys Lys Leu Lys Glu Leu Arg Glu Gln Pro Asn Leu Phe Ser Ile Leu Asp Lys Gly Asp Val Ala Thr Asn Asn Pro Val Glu Glu Ser Asp Lys Ala Asn Lys Ile Gln Glu Pro Leu Pro

35 Tyr Val Val Lys Thr Gln Ile Asn Lys Ala Ser Met Ile Ser Arg Asp Pro Ile Glu Trp Ala Lys Tyr Leu Ser Phe Glu Lys Arg Val Tyr Lys 75 Asp Asn Ser Lys Glu Asp Val Asn Phe Phe Ala Asn Gly Glu Ile Lys 85 90 Glu Ser Ser Arg Val Tyr Glu Ala Asn Lys Glu Gly Phe Glu Arg Arg 105 Ile Thr Lys Arg Tyr Asp Leu Ile Asp Arg Asn Ile Asp Arg Asn Arg 120 Glu Phe Phe Ile Lys Glu Ile Glu Ile Leu Thr His Thr Asn Ser Leu 135 140 Lys Glu Leu Lys Glu Gln Gly Leu Glu Ile Gln Leu Thr His His Asn 150 155 50 Glu Thr His Lys Lys Ala Leu Glu Asn Gly Asn Glu Ile Val Lys Glu 170 Tyr Asp His Leu Lys Asp Ile Tyr Gln Glu Val Glu Arg Thr Lys Asp 185 Gly Gly Leu Val Arg Glu Ile Ile Pro Ser Ile Ser Ser Ala Glu Tyr

200

55

								*								
	Phe	Lys 210	Leu	Tyr	Asn	Lys	Leu 215	Pro	Phe	Glu	Ser	Ile 220		Asn	Glu	Asn
	Thr 225	Lys	Leu	Asn	Thr	Asn 230	Asp	Asn	Glu	Glu	Val 235	Lys	Lys	Leu	Glu	Phe
5	Glu	Leu	Ala	Lys	Glu 245		His	Ile	Leu		Leu	Glu	Gln	Gln		240 Leu
	Ser	Ala	Thr	Asn 260		Tyr	Ser	Trp		250 Asp	Lys	Asp	Asp		255 Ala	Asn
10	Phe	Ala	Trp 275		Met	His	Årg		265 Ile	Asn	Glu	Asn			Lys	Glu
10	Asn	His 290		Ser	Ala	Asn	Asn	280 Ala	Asn	Lys	Ile		285 Gln	Phe	Phe	Phe
	Asn		Gly	Ser	Ile	Leu	295 Gly	Trp	Thr	Lys	Glu	300 Glu	Gln	Ser	Ala	Ile
1.5	305					310					315					320
15					325					330					335	Glu
				340					345					350		Val
20			355					360					365			Glu
		370					375					380				Tyr
	Asp	Lys	Leu	Val	Ser	Leu	Ser	Ala	Ala	Ile	Ile	Gln	Ala	Lys	Glu	Gly
25	385 Glv	Asn	Glu	Ara	Pro	390 Asn	Ser	Sor	. דת	7 an	395	7		Pro		400
	1		014	9	405	ADII.	Ser	ser	мта	410	ASI	Asn	Asn	Pro	11e 415	Lys
	Asn	Thr	Ile	Glu 420	Thr	Asn	Thr	Ser	Asn 425	Asn	Ile	Ile	Gln	Asn 430	Asn	Asp
30	Asn	Ile	Ile 435	Ile	Gln	Ile				٠		•		430		
	(2)	INFO	RMAT	ION	FOR	SEQ	ID N	IO:14	6:							
		(i)				ARAC										
35	1.					: 21 amin			acid	ls .						
						GY:										
Ю		(ii)	MOI	ECUL	E TY	PE:	prot	ein								
	. (	iii)	HYP	OTHE	TICA	L: Y	ES									
		(vi)				URCE										
5			(24	., OR	.GALVI	SM:	uett	coba	cter	ьхт	ori					
		(ix)	FEA (A	) NA	ME/K	EY:	misc	_fea	ture						•	
Λ		,				ON 1										
0.									EQ I							
	Met (				5					10					15	
5	Leu	сту (	GTA .	Tyr : 20	Leu l	Met 1	His :	Ile .	Ala :	Ile :	Phe	Ile	Ile	Phe	Ile	Trp

-	Ile	Gly	Gly 35	Leu	Lys	Phe	Val	Pro	Tyr	Glu	Ala	Glu	Gly 45	Ile	Ala	Pro
	Phe	Val		Asn	Ser	Pro	Phe 55	Phe	Ser	Phe	Met	Tyr 60		Phe	Glu	Lys
5	Pro 65	Ala	Tyr	Lys	Gln	His 70	Lys	Met	Ser	Glu	Ser 75		Ser	Met	Gln	Glu 80
					85			Ile		90					95	
10				100	•			Ala	105					110		
	•		115					Leu 120					125		. •	_
15		130					135	Ala				140				
13	145					150		Val	•		155	•				160
					165			Val Phe		170					175	
20				180		•		Arg	185					190		-
	•		195			Cys.		200	Je.	261	Val	GIY	205	пур	1111	пув
25		210			-1-		215									
	(2)	INFO	RMAT	MOI	FOR	SEQ	ID N	10:14	17:							
30		(i)	( <i>P</i> (E	A) LE B) TY C) SI	NGTH PE: RAND	I: 20 nucl EDNE	bas eic SS:	STIC se pa acid doub ular	irs l ole							
35		(ii)	MOI	ECUL	E TY	PE:	DNA	(gen	omic	:)						
	. (	iii)	HYP	OTHE	TICA	L: N	O							٠		
		(iv)	ANT	'I-SE	NSE:	NO										
40		(vi)				URCE SM:		coba	cter	pyl	ori			-		
45		(ix)	(A		ME/K	EY: ON 1		_fea 0	ture	:						
		(xi)	SEQ	UENC	E DE	SCRI	PTIO	N: S	EQ I	D, NO	:147	:				

TATACCATGG TGGGCGCTAA

50

- (2) INFORMATION FOR SEQ ID NO:148:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 23 base pairs
- 55 (B) TYPE: nucleic acid

	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
5	(ii) MOLECULE TYPE: DNA (genomic)	
3	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
10	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:	
20	ATGAATTCGA GTAAGGATTT TTG  (2) INFORMATION FOR SEQ ID NO:149:	23
25	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
35	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
40	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 122</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:	•
45	TTAACCATGG TGAAAAGCGA TA	22
	(2) INFORMATION FOR SEQ ID NO:150:	
50	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
55	(ii) MOLECULE TYPE: DNA (genomic)	

	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 123	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:150:	
15	TAGAATTC	CGC ATAACGATCA ATC	23
13	(2) INFO	ORMATION FOR SEQ ID NO:151:	
20	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
25	(ii)	MOLECULE TYPE: DNA (genomic)	
23	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
30	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
<b>35</b> .	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122	•
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:151:	
40	ATATCCAT	GG TGAGTTTGAT GA	22
	(2) INFO	ORMATION FOR SEQ ID NO:152:	
45	<b>(i)</b>	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
50	(ii)	MOLECULE TYPE: DNA (genomic)	
<i>-</i>	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	

	(A) ORGANISM: Helicobacter pylori		
5	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 125</pre>		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:		
10	ATGAATTCAA TTTTTTATTT TGCCA	•	25
10	(2) INFORMATION FOR SEQ ID NO:153:		
15	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 21 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
20	(ii) MOLECULE TYPE: DNA (genomic)		
20	(iii) HYPOTHETICAL: NO		
	(iv) ANTI-SENSE: NO		
25	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	1. 1	
30	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 121</pre>		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:		
35	AATTCCATGG TGGGGGCTAT G		21
	(2) INFORMATION FOR SEQ ID NO:154:		
40	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
.45	(ii) MOLECULE TYPE: DNA (genomic)		
43	(iii) HYPOTHETICAL: NO		
	(iv) ANTI-SENSE: NO		
50	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori		
55	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>		•

	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:154:		
_	ATGAATTC	TC GAȚAGCCAAA ATC		23
5	(2) INFO	RMATION FOR SEQ ID NO:155:		
	(i)	SEQUENCE CHARACTERISTICS:		
10		(A) LENGTH: 25 base pairs		
10		(B) TYPE: nucleic acid (C) STRANDEDNESS: double		
		(D) TOPOLOGY: circular		
		(b) Topologi. Circular		*
15	(ii)	MOLECULE TYPE: DNA (genomic)		
13	.(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
	•		•	
20	(vi)	ORIGINAL SOURCE:	•	
		(A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
		(A) NAME/KEY: misc_feature		
25		(B) LOCATION 125		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:155:		
•	AATTCCAT	GG TGCATAACTT CCATT		25
30	(2) INFO	RMATION FOR SEQ ID NO:156:		
	121	CHOIVENON CHARACTER TOTAL		
	(1)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 25 base pairs		
35		(B) TYPE: nucleic acid		
		(C) STRANDEDNESS: double		
•	•	(D) TOPOLOGY: circular		
	(ii)	MOLECULE TYPE: DNA (genomic)		
40			•	
	(111)	HYPOTHETICAL: NO		
•	(iv)	ANTI-SENSE: NO		
45	(vi)	ORIGINAL SOURCE:	•	
		(A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
	•	(A) NAME/KEY: misc_feature		
50		(B) LOCATION 125		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:156:	·	

	(2) INFORMATION FOR SEQ ID NO:157:	
5	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 24 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
10	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	•
15	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
	(ix) FEATURE:	
20	(A) NAME/KEY: misc_feature (B) LOCATION 124	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:157:	
25	ATTTCCATGG TCATGTCTCA TATT	2
	(2) INFORMATION FOR SEQ ID NO:158:	
٠.	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 23 base pairs	
30	(B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: circular	
35	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
40	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	,
	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature</pre>	
15	(B) LOCATION 123	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:	
50	ATGAATTCCA TCTTTTATTC CAC	23
-	(2) INFORMATION FOR SEQ ID NO:159:	
	(i) SEQUENCE CHARACTERISTICS:	
5	(A) LENGTH: 27 base pairs	

	•	(C) STRANDEDNESS: double (D) TOPOLOGY: circular		
5	(ii)	MOLECULE TYPE: DNA (genomic)		
,	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO	·	•
10	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
15	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 127		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:159:		
20	AACCATGG'	TG ATTTTAAGCA TTGAAAG		27
	(2) INFO	RMATION FOR SEQ ID NO:160:		•
25	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 28 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
30		MOLECULE TYPE: DNA (genomic)		
		HYPOTHETICAL: NO		
2.5		ANTI-SENSE: NO		•
35	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
40	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 128		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:160:		
45	AAGAATTC	CA CTCAAAATTT TTTAACAG		28
45	(2) INFOR	RMATION FOR SEQ ID NO:161:	•	
50	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
55	(ii)	MOLECULE TYPE: DNA (genomic)		

	(iii)	HYPOTHETICAL: NO	
٠,	(iv)	ANTI-SENSE: NO	
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 125	;
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:161:	
15		T ATGTTATCTT CTAAT  MATION FOR SEQ ID NO:162:	
	·		•
20		SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	••
25		MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
30	•	ANTI-SENSE: NO  ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
	( d as)		
35	(1x)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 123	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:162:	
40	TGAATTCAA	C CATTTTAACC CTG	. 2
	(2) INFOR	MATION FOR SEQ ID NO:163:	
45	<b>(i)</b>	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 27 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
50	(ii)	MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

		(A) ORGANISM: Helicobacter pylori	•	
5	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 127		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:163:		•
10	TATACCATO	G TGAAATTTT TCTTTTA		27
,10	(2) INFOR	MATION FOR SEQ ID NO:164:		
15.	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
20	(ii)	MOLECULE TYPE: DNA (genomic)		
20	(iii)	HYPOTHETICAL: NO	·	
	(iv)	ANTI-SENSE: NO		
25	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
30	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 125		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:164:		
35	AGAATTCA	AT TGCGTCTTGT AAAAG		25
	(2) INFO	RMATION FOR SEQ ID NO:165:		
40	. (i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 24 base pairs  (B) TYPE: nucleic acid		
·		(C) STRANDEDNESS: double (D) TOPOLOGY: circular		
45	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
50	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
. 55	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 124		

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:	
5	TATACCATGG TGATGGACAA ACTC	24
	(2) INFORMATION FOR SEQ ID NO:166:	
10	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 23 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>	
15	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
20	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
25	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>	·
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:	
30	ATGAATTCCC ACTTGGGGCG ATA	23
	(2) INFORMATION FOR SEQ ID NO:167:	
35	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
40	(ii) MOLECULE TYPE: DNA (genomic)	``
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
45	(vi) ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
50	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 125</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:	
55	TTATGGATCC AAACCAATTA AAACT	25

	(2) INFORMATION FOR SEQ ID NO:168:	•	
5	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 23 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>		
10	(ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO		
15	<pre>(iv) ANTI-SENSE: NO  (vi) ORIGINAL SOURCE:</pre>		· .
20	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 123</pre>		
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:  TATCTCGAGT TATAGAGAAG GGC  (2) INFORMATION FOR SEQ ID NO:169:		23
30	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 22 base pairs</li><li>(B) TYPE: nucleic acid</li><li>(C) STRANDEDNESS: double</li><li>(D) TOPOLOGY: circular</li></ul>		
35	(ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO		
	(iv) ANTI-SENSE: NO		
40	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>		
45	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 122</pre>		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:169:		
50	TTAACCATGG TGAAAAGCGA TA (2) INFORMATION FOR SEQ ID NO:170:		22
55	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 24 base pairs</li><li>(B) TYPE: nucleic acid</li></ul>		

		(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
5	(ii)	MOLECULE TYPE: DNA (genomic)	
	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
10	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
15	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 124	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:170:	
20	••	GC CTCTAAAACT TTAG RMATION FOR SEQ ID NO:171:	2
25		SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
30	. 00	MOLECULE TYPE: DNA (genomic)	· .
	(iii)	HYPOTHETICAL: NO	
35		ANTI-SENSE: NO ORIGINAL SOURCE:	
	( \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	(A) ORGANISM: Helicobacter pylori	
40	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:171:	
45	TTAACCATO	GG TGAAAAGCGA TA	2:
٠.	(2) INFO	RMATION FOR SEQ ID NO:172:	
50	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
55	(ii)	MOLECULE TYPE: DNA (genomic)	

	(iii)	HYPOTHETICAL: NO			
	(iv)	ANTI-SENSE: NO	• •	•	
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori			
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 123			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:172:			
15	TAGAATTC	GC ATAACGATCA ATC			23
13	(2) INFO	RMATION FOR SEQ ID NO:173:			•
20	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		.*	
25	(ii)	MOLECULE TYPE: DNA (genomic)			
23	(iii)	HYPOTHETICAL: NO			
	(iv)	ANTI-SENSE: NO			
30	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori			
35	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:173:			
40	ATATCCAT	GG TGAGTTTGAT GA			22
	(2) INFO	RMATION FOR SEQ ID NO:174:			
45	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular			
50	(ii)	MOLECULE TYPE: DNA (genomic)			
)U	(iii)	HYPOTHETICAL: NO	•		
	(iv)	ANTI-SENSE: NO			
55	· (3ri)	ORIGINAL SOURCE			

		(A) ORGANISM: Helicobacter pylori			
•	(ix)	FEATURE:			
5		<ul><li>(A) NAME/KEY: misc_feature</li><li>(B) LOCATION 125</li></ul>			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:174:			
		AA TTTTTATTT TGCCA			
10			*	X	25
	(2) INFC	RMATION FOR SEQ ID NO:175:			
	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs			
15		(B) TYPE: nucleic acid			
		(C) STRANDEDNESS: double			
•		(D) TOPOLOGY: circular			
20	(ii)	MOLECULE TYPE: DNA (genomic)			
	(iii)	HYPOTHETICAL: NO			
	(iv)	ANTI-SENSE: NO			
25	(vi)	ORIGINAL SOURCE:			
		(A) ORGANISM: Helicobacter pylori			
	(ix)	FEATURE:			
20		<pre>(A) NAME/KEY: misc_feature</pre>			
30		(B) LOCATION 123			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:175:	•		
35	AATTCCAT	GG CTATCCAAAT CCG			23
	(2) INFO	RMATION FOR SEQ ID NO:176:			
	. (i)	SEQUENCE CHARACTERISTICS:	7		
40	·	(A) LENGTH: 25 base pairs			
40	-	(B) TYPE: nucleic acid			
	•	(C) STRANDEDNESS: double			
	•	(D) TOPOLOGY: circular		•	
45	(ii)	MOLECULE TYPE: DNA (genomic)			
	(iii)	HYPOTHETICAL: NO			
	(iv)	ANTI-SENSE: NO			
50	(vi)	ORIGINAL SOURCE:			
		(A) ORGANISM: Helicobacter pylori			
	(ix)	FEATURE:			
55		(A) NAME/KEY: misc_feature			

WO 98/18323 PCT/US97/19575

- 241 -

	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:176:		
5	ATGAATTC	CGC CAAAATCGTA GTATT		25
,	(2) INFO	DRMATION FOR SEQ ID NO:177:		
٠.	(i)	SEQUENCE CHARACTERISTICS:		
10		(A) LENGTH: 24 base pairs (B) TYPE: nucleic acid		
10		(C) STRANDEDNESS: double		
	•	(D) TOPOLOGY: circular		
15	(ii)	MOLECULE TYPE: DNA (genomic)		
1,3	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
20	(vi)	ORIGINAL SOURCE:		
	, (,-,	(A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
_		(A) NAME/KEY: misc_feature		
25		(B) LOCATION 124		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:177:		
30	GATACCAT	GG AATTTATGAA AAAG		24
30	(2) INFO	ORMATION FOR SEQ ID NO:178:		
	(i)	SEQUENCE CHARACTERISTICS:		
		(A) LENGTH: 25 base pairs		
35		(B) TYPE: nucleic acid		
		(C) STRANDEDNESS: double (D) TOPOLOGY: circular		
	•	(2) ISTOLOGI. CIICUIUI		
40	(ii)	MOLECULE TYPE: DNA (genomic)		
40	' (iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
45	(vi)	ORIGINAL SOURCE:		
		(A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
εń		(A) NAME/KEY: misc_feature		
50		(B) LOCATION 125		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:178:	•	

55

	(2) INFO	RMATION FOR SEQ ID NO:179:		
5	. <b>(i)</b>	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 19 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
10	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO	•	
	(iv)	ANTI-SENSE: NO		
15	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		<b>.</b>
20	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 119		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:179:		
25		TT TAGAAATCG  RMATION FOR SEQ ID NO:180:		. 1
30	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 20 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
35	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
40	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
45	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 120		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:180:		
50	ATTTCAACC	A ATTCAATGCG		20
	(2) INFOR	MATION FOR SEQ ID NO:181:		
55	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 20 base pairs (B) TYPE: nucleic acid		

		(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
5	(ii)	MOLECULE TYPE: DNA (genomic)	
3	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
10	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
15	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 120	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:181:	
20		TG ATTTGAAGCT  RMATION FOR SEQ ID NO:182:	20
25	<b>(i)</b>	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
30		MOLECULE TYPE: DNA (genomic) HYPOTHETICAL: NO	
		ANTI-SENSE: NO	
35	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
40	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 122	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:182:	
45		AG ATACCAAGAA GT RMATION FOR SEQ ID NO:183:	. 22
50	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 22 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
55	(ii)	MOLECULE TYPE: DNA (genomic)	

	(iii)	HYPOTHETICAL: NO		:	
	(iv)	ANTI-SENSE: NO			
5	(vi)	ORIGINAL SOURCE:			
		(A) ORGANISM: Helicobacter pyl	.ori		
	(ix)	FEATURE: (A) NAME/KEY: misc_feature			•
10		(B) LOCATION 122			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO	:183:		
15	CTTGAATT	TAG GGGCAAAGAT CG			22
	(2) INFO	RMATION FOR SEQ ID NO:184:			
	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 22 base pairs			• •
20		(B) TYPE: nucleic acid			
	,	(C) STRANDEDNESS: double			
		(D) TOPOLOGY: circular			
25	(ii)	MOLECULE TYPE: DNA (genomic)			
	(iii)	HYPOTHETICAL: NO			
	(iv)	ANTI-SENSE: NO			
30	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pyl	ori		
	(ix)	FEATURE: (A) NAME/KEY: misc_feature			
35		(B) LOCATION 122			
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO	:184:		
40	ATGCGTTT	TT ACCCAAAGAA GT			22
	(2) INFO	RMATION FOR SEQ ID NO:185:			
	(i)	SEQUENCE CHARACTERISTICS:			
45		(A) LENGTH: 22 base pairs	. •	•	
43	<b>:</b>	(B) TYPE: nucleic acid			
		(C) STRANDEDNESS: double (D) TOPOLOGY: circular			
				•	
50	•	MOLECULE TYPE: DNA (genomic)			
		HYPOTHETICAL: NO			•
	(iv)	ANTI-SENSE: NO			

•		(A) ORGANISM: Helicobacter pylori	•	-
	(ix)	FEATURE:		
5		(A) NAME/KEY: misc_feature (B) LOCATION 122		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:185:	•	•
10	ATAACGCC	AC TTCCTTATTG GT		22
	(2) INFO	RMATION FOR SEQ ID NO:186:		
15	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 19 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double		
		(D) TOPOLOGY: circular		
20	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		-
25	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
30	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 119		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:186:	•	
35	CTTTGGGT	AA AAACGCATC		19
, ,	(2) INFO	RMATION FOR SEQ ID NO:187:		
10	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 20 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
15	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO	÷	
0	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
5	(ix)	FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 1 20		

55

	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:187:		
5	CGATCTTT	GA TCCTAATTCA		20
<b>.</b>	(2) INFO	ORMATION FOR SEQ ID NO:188:		
	(i)	SEQUENCE CHARACTERISTICS:		
10		(A) LENGTH: 19 base pairs		
10		(B) TYPE: nucleic acid		
		(C) STRANDEDNESS: double (D) TOPOLOGY: circular		
		(b) Torobodi: Circular		
15	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		*
20	(vi)	ORIGINAL SOURCE:	•	
		(A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
		(A) NAME/KEY: misc_feature		
25		(B) LOCATION 119		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:188:		
30	ATCAAGTT	GC CTATGCTGA		19
	(2) INFO	RMATION FOR SEQ ID NO:189:		
	(i)	SEQUENCE CHARACTERISTICS:		
		(A) LENGTH: 22 base pairs		
35		(B) TYPE: nucleic acid		
		(C) STRANDEDNESS: double		
		(D) TOPOLOGY: circular		
40	(ii)	MOLECULE TYPE: DNA (genomic)	• .	
	(iii)	HYPOTHETICAL: NO	•	
	(iv)	ANTI-SENSE: NO		
45 .	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
•		PILOLI		
	(ix)	FEATURE:	•	
50		(A) NAME/KEY: misc_feature		1
50		(B) LOCATION 122		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:189:	•	

	(Z) INFOR	dualion for SEQ ID NO:190:		
5	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 23 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular		
10	(ii)	MOLECULE TYPE: DNA (genomic)		
-	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
15	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
20	(ix)	FEATURE:  (A) NAME/KEY: misc_feature  (B) LOCATION 123		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:190:		
25	GGATTATGC	G ATTGTTTTAC AAG		2
	(2) INFOR	MATION FOR SEQ ID NO:191:		
30	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 21 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	•	
35	(ii)	MOLECULE TYPE: DNA (genomic)	• •	•
	(iii)	HYPOTHETICAL: NO		
40	(vi)	ANTI-SENSE: NO ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
		FEATURE:		
45		(A) NAME/KEY: misc_feature (B) LOCATION 121		•
-	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:191:	,	
50	GTCTTTAGC	A AAAATGGCGT C		21
	(2) INFOR	MATION FOR SEQ ID NO:192:		
	(i) s	SEQUENCE CHARACTERISTICS: (A) LENGTH: 21 base pairs		
55		(B) TYPE: nucleic acid	·.	

		(C) STRAND (D) TOPOLO						
5	(ii)	MOLECULE TY	PE: DNA	(genomic)				
	(iii)	нуротнетіса	L: NO	•				
	(iv)	ANTI-SENSE:	NO			•		
10	(vi)	ORIGINAL SO (A) ORGANI		cobacter	pylori			
15	(ix)	FEATURE: (A) NAME/K (B) LOCATI	EY: misc ON l2	_feature 1				
1.	(xi)	SEQUENCE DE	SCRIPTION	N: SEQ II	NO:192:			•
20	•	A AGAGAGCCT						21
		MATION FOR SEQUENCE CH	ARACTERIS	STICS:				
25		(A) LENGTH (B) TYPE: (C) STRAND (D) TOPOLO	nucleic a	acid double				
30	•	MOLECULE TY		(genomic)				
	(iii)	HYPOTHETICA	L: NO					
	(iv)	ANTI-SENSE:	NO					
35	(vi)	ORIGINAL SO (A) ORGANI		obacter	pylori			
	(ix)	FEATURE:						
40	- 10	(A) NAME/KI	Y: misc_ ON 118	_feature	*			
	(xi)	SEQUENCE DE	CRIPTION	: SEQ ID	NO:193:			
45	CTTATGGGG	G TATTGTCA						18
43	(2) INFOR	MATION FOR S	SEQ ID NO	:194:				,
50	<b>(1)</b>	(A) LENGTH (B) TYPE: I (C) STRANDI (D) TOPOLOG	: 18 base nucleic a EDNESS: d	pairs cid ouble				
<i></i>	(ii) 1	MOLECULE TY	PE: DNA (	genomic)				

	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
5	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
10	(ix)	FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 118	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:194:	
15	AGCATGTG	GG TATCCAGC	18
13	(2) INFO	RMATION FOR SEQ ID NO:195:	
20	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 19 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
25	(ii)	MOLECULE TYPE: DNA (genomic)	
23	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
30	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori	
35		FEATURE: (A) NAME/KEY: misc_feature (B) LOCATION 119	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:195:	•
40		GC CTAAAGACT  RMATION FOR SEQ ID NO:196:	19
45		SEQUENCE CHARACTERISTICS:  (A) LENGTH: 18 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
50	(ii)	MOLECULE TYPE: DNA (genomic)	•
.50	(iii)	HYPOTHETICAL: NO	
	(iv)	ANTI-SENSE: NO	
55	(vi)	ORIGINAL SOURCE:	

			· ·	
	-	(A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
5		(A) NAME/KEY: misc_feature (B) LOCATION 118		
*	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:196:		
10	CTGCCTCC	AC CTTTGATC		18
	(2) INFO	RMATION FOR SEQ ID NO:197:		
ė	(i)	SEQUENCE CHARACTERISTICS: (A) LENGTH: 19 base pairs		
15	•	(B) TYPE: nucleic acid		
		(C) STRANDEDNESS: double	•	
		(D) TOPOLOGY: circular		
20	(ii)	MOLECULE TYPE: DNA (genomic)		
20	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
25	(vi)	ORIGINAL SOURCE:		
		(A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
20		(A) NAME/KEY: misc_feature		
30		(B) LOCATION 119		
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:197:		
35	ACCAATAT	CA ATTGGCACT		19
	(2) INFO	RMATION FOR SEQ ID NO:198:		
	(i)	SEQUENCE CHARACTERISTICS:		
40		(A) LENGTH: 18 base pairs		
40		(B) TYPE: nucleic acid	•	
		(C) STRANDEDNESS: double		
		(D) TOPOLOGY: circular	•	
45	(ii)	MOLECULE TYPE: DNA (genomic)		
	(iii)	HYPOTHETICAL: NO		
	(iv)	ANTI-SENSE: NO		
50	(vi)	ORIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori		
	(ix)	FEATURE:		
		(A) NAME/KEY: misc_feature		
55		(B) LOCATION 1 18		

	(xi) SEQUEN	CE DESCRIPTION: S	EQ ID NO:198:		
5	ACTTGGAAAA GCTC	rgca			18
3	(2) INFORMATION	FOR SEQ ID NO:19	9:	*	
10	(A) L (B) T (C) S	CE CHARACTERISTIC ENGTH: 19 base pa VPE: nucleic acid TRANDEDNESS: doub DPOLOGY: circular	irs		÷
15	(ii) MOLECU	LE TYPE: DNA (gen	omic)		
,	(iii) HYPOTH	ETICAL: NO			
	(iv) ANTI-S	ENSE: NO			* *
20	(vi) ORIGINA (A) OI	AL SOURCE: RGANISM: Helicoba	cter pylori		
25		R: MME/KEY: misc_fea DCATION 119	ture		
	(xi) SEQUENC	CE DESCRIPTION: S	EQ ID NO:199:		
30	CTTGCTTGTC ATAT		_		19
	•	FOR SEQ ID NO:20			
35	(A) Li (B) T (C) S	E CHARACTERISTIC INGTH: 18 base pa TPE: nucleic acid TRANDEDNESS: doub DPOLOGY: circular	irs		
40	(ii) MOLECUI	E TYPE: DNA (gen	omic)		
	(iii) HYPOTHI	TICAL: NO			
	(iv) ANTI-SI	INSE: NO			
45		L SOURCE: GANISM: Helicoba	cter pylori		
50		: ME/KEY: misc_fea CATION 118	ture		
	(xi) SEQUENC	E DESCRIPTION: S	EQ ID NO:200:		
55	GTTGAAGTGT TGGTG	CTA			18

	(2) INFORMATION FOR SEQ ID NO:201:		
5	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 22 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>		
10	(ii) MOLECULE TYPE: DNA (genomic)		
	(iii) HYPOTHETICAL: NO		
	(iv) ANTI-SENSE: NO		
15	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>		
20	<pre>(ix) FEATURE:           (A) NAME/KEY: misc_feature           (B) LOCATION 122</pre>		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:201:	÷	
25	CAAGCAAGTG GTTTGGTTTT AG  (2) INFORMATION FOR SEQ ID NO:202:		22
30	<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 22 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: double</li> <li>(D) TOPOLOGY: circular</li> </ul>		· .
35	(ii) MOLECULE TYPE: DNA (genomic)		,
	(iii) HYPOTHETICAL: NO		
40	<ul><li>(iv) ANTI-SENSE: NO</li><li>(vi) ORIGINAL SOURCE:</li><li>(A) ORGANISM: Helicobacter pylori</li></ul>		·
45	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 122</pre>		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:202:		
50	TGGAAAGAGC AAATCATTGA AG		22
	(2) INFORMATION FOR SEQ ID NO:203:		
55	<ul><li>(i) SEQUENCE CHARACTERISTICS:</li><li>(A) LENGTH: 21 base pairs</li><li>(B) TYPE: nucleic acid</li></ul>		

	(C) STRANDEDNESS: double (D) TOPOLOGY: circular	
5	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
10	(vi) ORIGINAL SOURCE:  (A) ORGANISM: Helicobacter pylori	
15	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature     (B) LOCATION 121</pre>	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:203:	
20	GCCCATAATC AAAAAGCCCA T (2) INFORMATION FOR SEQ ID NO:204:	21
	(i) SEQUENCE CHARACTERISTICS:	
<b>25</b> <sup>2</sup>	(A) LENGTH: 24 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: doublé (D) TOPOLOGY: circular	
30	(ii) MOLECULE TYPE: DNA (genomic)	
	(iii) HYPOTHETICAL: NO	
	(iv) ANTI-SENSE: NO	
35	<pre>(vi) ORIGINAL SOURCE:     (A) ORGANISM: Helicobacter pylori</pre>	
	<pre>(ix) FEATURE:     (A) NAME/KEY: misc_feature</pre>	
40	(B) LOCATION 124	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:204:	
45	CTAAAACCAA ACCACTTGCT TGTC	24
	(2) INFORMATION FOR SEQ ID NO:205:	
50	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 16 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular	
55	(ii) MOLECULE TYPE: DNA (genomic)	

	(iii) H	YPOTHETICAL: NO			
	(iv) A	NTI-SENSE: NO			
5		RIGINAL SOURCE: (A) ORGANISM: Helicobacter pylori			
10	(ix) F	EATURE: (A) NAME/KEY: misc_feature (B) LOCATION 116		-	
	(xi) S	EQUENCE DESCRIPTION: SEQ ID NO:205:			
15	GTAAAACGAC	GGCCAG  ATION FOR SEQ ID NO:206:		•	16
20		EQUENCE CHARACTERISTICS:  (A) LENGTH: 17 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular			
25		OLECULE TYPE: DNA (genomic)			
		YPOTHETICAL: NO			`
30	(vi) 0	NTI-SENSE: NO			
35	(ix) F	(A) ORGANISM: Helicobacter pylori EATURE: (A) NAME/KEY: misc_feature (B) LOCATION 117			
	CAGGAAACAG	EQUENCE DESCRIPTION: SEQ ID NO:206:			
40		ATION FOR SEQ ID NO:207:			17
45		EQUENCE CHARACTERISTICS:  (A) LENGTH: 21 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: double  (D) TOPOLOGY: circular			
50	•	DLECULE TYPE: DNA (genomic)			
		POTHETICAL: NO			
		TI-SENSE: NO			
<b>55</b> .	(vi) OR	IGINAL SOURCE:			

(vi) ORIGINAL SOURCE:

15

20

(A)	ORGANISM:	Helicobacter	pylori
-----	-----------	--------------	--------

#### (ix) FEATURE:

- (A) NAME/KEY: misc\_feature
- 5 (B) LOCATION 1...21
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:207:

### ATCTTACCTA TCACCTCAAA T

21

(2) INFORMATION FOR SEQ ID NO:208:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: circular
- (ii) MOLECULE TYPE: DNA (genomic)
  - (iii) HYPOTHETICAL: NO
    - (iv) ANTI-SENSE: NO
- 25 (vi) ORIGINAL SOURCE:
  - (A) ORGANISM: Helicobacter pylori
  - (ix) FEATURE:
    - (A) NAME/KEY: misc\_feature
- 30 (B) LOCATION 1...21
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:208:

AGACAGCAAC ATCTTTGTGA A

### **CLAIMS**

- An isolated nucleic acid comprising a nucleotide sequence encoding an
   H. pylori polypeptide at least about 60% homologous to an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
- An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
  - 3. An isolated nucleic acid which encodes an *H. pylori* polypeptide, comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
    - 4. The isolated nucleic acid of claim 1, comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.

5. An isolated nucleic aci

5. An isolated nucleic acid molecule encoding an *H. pylori* polypeptide, comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.

25

15

6. An isolated nucleic acid comprising a nucleotide sequence of at least 8 nucleotides in length, wherein the sequence hybridizes under stringent hybridization conditions to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.

30 ·

7. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID

NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21, or a complement thereof.

- 8. The isolated nucleic acid of claim 7, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48, or a complement thereof.
- The isolated nucleic acid of claim 7, wherein said H. pylori cell envelope
   polypeptide or a fragment thereof is an H. pylori outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71, or a complement thereof.
- The isolated nucleic acid of claim 9, wherein said H. pylori outer membrane polypeptide or a fragment thereof is an H. pylori polypeptide having a
  terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO:71, or a complement thereof.
- The isolated nucleic acid of claim 9, wherein said H. pylori outer membrane polypeptide or a fragment thereof is an H. pylori polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, or a complement thereof.
- 12. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO:

WO.98/18323 PCT/US97/19575

101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

5

13. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.

10

15

14. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.

20

15. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO:144.

25

30

16. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ ID NO: 131.

35

17. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ ID NO: 20, SEQ

ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68, or a complement thereof.

- 18. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* secreted polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.
- 19. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50,
  20 SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73, or a complement thereof.
- An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori cellular polypeptide or a fragment thereof selected from the group consisting
  of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.
- 21. A probe comprising a nucleotide sequence consisting of at least 8

  30 nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NO:

  1-SEQ ID NO: 73, or a complement thereof.
- 22. A recombinant expression vector comprising the nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19 or 20 operably linked to a transcription regulatory element.

20

35

- 23. A cell comprising a recombinant expression vector of claim 22.
- 24. A method for producing an *H. pylori* polypeptide comprising culturing a cell of claim 23 under conditions that permit expression of the polypeptide.

25. The method of claim 24, further comprising purifying the polypeptide from the cell.

- 26. A method for detecting the presence of a *Helicobacter* nucleic acid in a sample comprising:
  - (a) contacting a sample with a nucleic acid of any of claims 6 or 21 so that a hybrid can form between the probe and a *Helicobacter* nucleic acid in the sample; and
- (b) detecting the hybrid formed in step (a), wherein detection of a hybrid indicates the presence of a *Helicobacter* nucleic acid in the sample.
  - 27. An isolated *H. pylori* polypeptide comprising an amino acid sequence at least about 60% homologous to an *H. pylori* polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
  - 28. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.
- 25 29. The isolated *H. pylori* polypeptide of claim 28, wherein said polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.
- 30. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid which hybridizes under stringent hybridization conditions to a nucleic acid selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
  - 31. An isolated *H. pylori* polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
  - 32. An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 76, SEQ

WO 98/18323 PCT/US97/19575

ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

- 33. The isolated polypeptide of claim 32, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.
- 34. The isolated polypeptide of claim 32, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.
  - 35. The isolated polypeptide of claim 34, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO:144.

25

36. The isolated polypeptide of claim 34, wherein said *H. pylori* outer
30 membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a
terminal phenylalanine residue or a fragment thereof selected from the group consisting
of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO:
80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO:
101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ
35 ID NO: 131.

An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21.

10

38. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48.

15

20

39. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71.

25

40. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO:71.

30

35

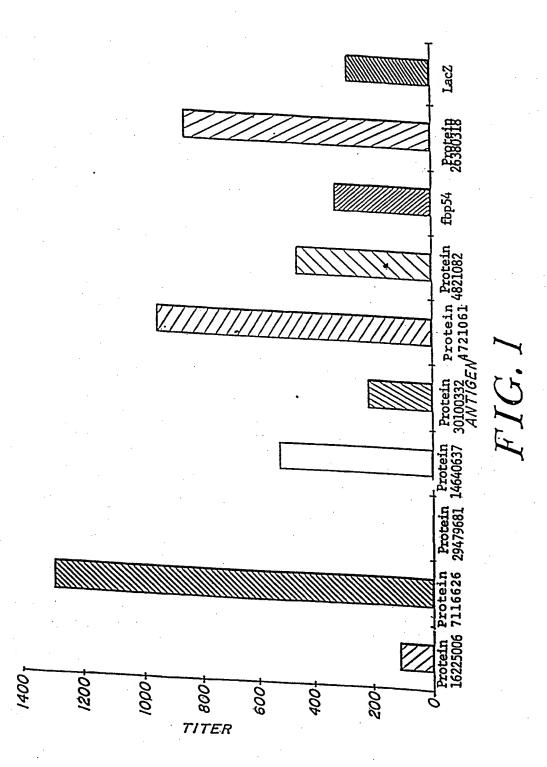
41. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58.

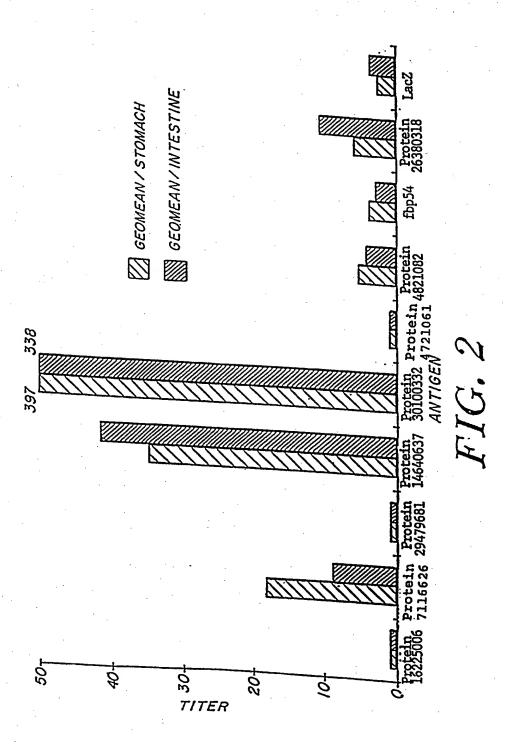
- 42. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.
- 43. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ
  10 ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73.
- 44. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.
- 45. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68.
  - 46. A fusion protein comprising an *H. pylori* polypeptide which comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 operatively linked to a non-*H. pylori* polypeptide.

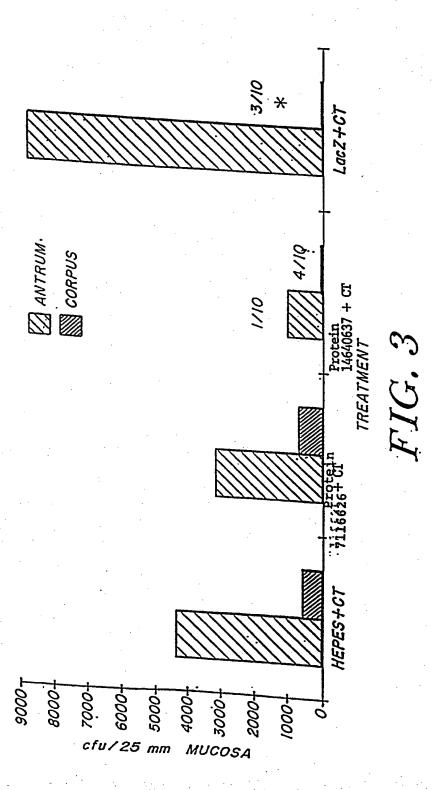
- 47. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one isolated nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19, or 20.
- 5 48. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one *H. pylori* polypeptide or a fragment thereof of any of claims 26, 27, 28, 29, 30, 31, 32, 37, 42, 43, 44 or 45.
- 49. A vaccine formulation of claim 47, further comprising a pharmaceutically acceptable carrier.
  - 50. A vaccine formulation of claim 48, further comprising a pharmaceutically acceptable carrier.
- 15 51. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises an adjuvant.
  - 52. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises an adjuvant.
  - 53. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises a delivery system.
- 54. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises a delivery system.
  - 55. A vaccine formulation of claim 53, wherein the delivery system comprises a live vector.
- 30 56. A vaccine formulation of claim 54, wherein the delivery system comprises a live vector.
  - 57. A vaccine formulation of claim 55, wherein the live vector is a bacteria or a virus.
  - 58. A vaccine formulation of claim 56, wherein the live vector is a bacteria or a virus.

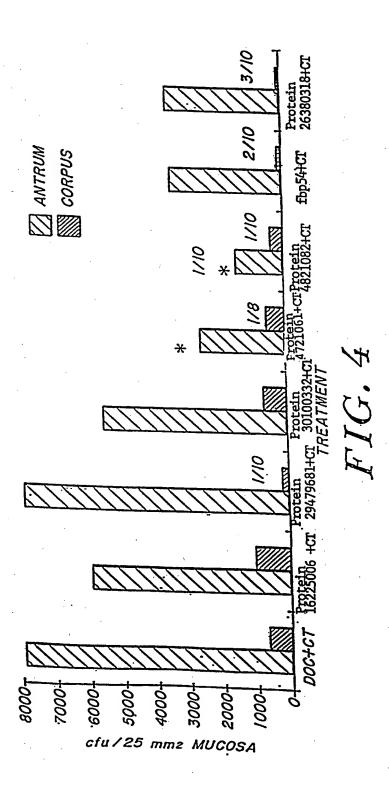
15

- 59. A vaccine formulation of claim 53, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.
- 5 60. A vaccine formulation of claim 54, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.
  - 61. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 47, such that treatment or reduction of risk of *H. pylori* infection occurs.
  - 62. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 48, such that treatment or reduction of risk of *H. pylori* infection occurs.
  - 63. A method of producing a vaccine formulation comprising: combining at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.
    - 64. A method of producing a vaccine formulation comprising:
  - (a) providing at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146; and
- (b) combining at least one said isolated *H. pylori* polypeptide or a fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.
  - 65. A method of producing a vaccine formulation comprising:
- (a) culturing a cell under condition that permit expression of an H.
   30 pylori polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146;
  - (b) isolating said *H. pylori* polypetide from said cell; and
- (c) combining at least one said isolated *H. pylori* polypeptide or a fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine
   formulation.









aa Se	gID#
74	T BLOCK A
115	MIKRIAC-ILSLSASLALAGEVNGFFMGAGYQQGRYGPYNSNY
87	MIKRIAC-ILSLSASLALAGEVNGFFMGAGYQQGRYGPYNSNY
116	MKKFFSQSLLAL-IISMNAVSGMDGNGVFLGAGYLQGDAQMHADIN
84	MKKFFSQSLLAL-IISMNAVSGMDGNGVFLGAGYLQGQAQMHADIN
;	MARULMKKFVALGLLSAVLSSSLLAEGIGVYIGTNYQLGPARLNSNIYNTGDCTGS
	* * . *
•	
74	BLOCK B BLOCK C
115	SDAWNESSKWFGARV
87	
116	SOMON THE GENERAL SOMON THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SOM THE SO
84	VVGCPPGLTANKHNPGGTNIATURGENANTIEGFDALLGYQFFFEKHFGLRL
	VVGCPPGLTANKHNPGGTNINWHSKYANGALDGFGLNVGYKKFFQFKSLDMTSKWFGFRV
74	YGFLUWFNTSGTEHT
115	YGFLUWFNTSGTEHTKTNLLTYGGGGD YGFLUWFNTSGTEHTKTNLLTYGGGGD
87	YGFFDYAHANSIKLKNPNYNSEAAQVASQILGKQEINRLTNIADPRTFEPNMLTYGGAMD
116	YGFFIYAHANSIKLKNPNYNSEAAQVASQILGKQEINRLTNIADPRTFEPNMLTYGGAMD YGLFIYGHADLGKONY
84	YGLFUYGHADLGKQVYAPNKIQLDMVSWGVGSD
	** *
•	BLOCK D
74	LIVNLIPLDKFALGLIGGVQLAGNTWMFPYDVNQ
115	LIVNLIPLDKFAIGLIGGVOLAGNTWMFPVDVNO
87	VIIVIVALMOLIMOLIGATIOLIAGNISMI.MATTICETTITICAT
116	**************************************
84	LLADIIDKDNASFGIFGGVAIGGNTWKSSAANYWKEQIIEAKGPDVCTPTYCNPNAPYST
	* * **. *
7.4	BLOCK E BLOCK F
115	THE QELWINLGGRMRVGDRSAFEAGUKEDMINIOC
87	THE THIRD GREEK VGDRSAFFAGVE PMONIOC - CONTROL TO THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY
116	ORDER OF DE INVORKURILKHSSIFACVKFDMI EVENDVID
84	TOTAL TOTAL CONTROL OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PRO
Q-2	THE CONTROL OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE PROPERTY OF
•	* ** *.
74	DYVFTF
115	DYVFTF
87.	NYVFTF
116	NYVFTF
84	GYNYTF
	* **

83	MRKLFIPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
89	
108	MRKLF,IPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
118	MRKLFIPLLLFSALEANEKNGFFIEAGPETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
83 89	ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
108	ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNT
.118	ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
83	IDLGVIETIPKHSKIVLPGEAFDSLKIDPYTLFLPKIEATSTSISDANTORVFET
89	VIETIPKHSKIVLPGEAFDSLKEAFDKIDPYTFFFFKFEATSTSISDTNIQRVFET
108	IDLGVIETIPKHSKIVLPGEAFDSLKEAFDKIDPYTLFLPKFEATSTSISDTNTORVFET
118	IDLGVIETIPKHSKIVLPGEAFDSLKIDPYTLFLPKIEATSTSISDANTQRVFET
ů.	***********
83	LNKIKTNLVVNYRNENKFKDHENHWEAFTPQTAEEFTNLMLNMIAVLDS
89	LNNIKTNLIMKYSNENPNNFNTCPYNNNGNTKNDCWQNFTPQTAEEFTNLMLNMIAVLDS
108	LNNIKTNLIMKYSNENPNNFNTCPYNNNGNTKNDCWQNFTPQTAEEFTNLMLNMIAVLDS
118	LNKIKTNLVVNYRNENKFKDHENHWEAFTPQTAEEFTNLMLNMIAVLDS
	* ***************
83	QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDQKYVLNKQDIVNKFKNKA
89	QSWGDAILNAPFEFTNSSTDCDSDPSKCVNPGVNGRVDTKVDQQYILNKQGIINNFRKKI
108	QSWGDAILNAPFEFTNSSTDCDSDPSKCVNPGVNGRVDTKVDQQYILNKQGIINNFRKKI
118	QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDQKYVLNKQDIVNKFKNKA
83	DLDVIVLKDSGVVGLGSDITPSNNDDGKHYGQLGVVASALDPKKLFGDNLKTINLEDLRT
89	EIDAVVLKNSGVVGLANGYGNDG-EYGTLGVEAYALDPKKLFGNDLKTINLEDLRT
108	EIDAVVLKNSGVVGLANGYGNDG-EYGTLGVEAYALDPKKLFGNDLKTINLEDLRT
118	DLDVIVLKDSGVVGLGSDITPSNNDDGKHYGQLGVVASALDPKKLFGDNLKTINLEDLRT
*	. * . * * * * * * * * * * * * * * * * *
83	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVC
89	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
108	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
118	ILHEFSHTKCYCHNCNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
	***********
83	
89	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTODL
108	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTODL
118	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTODL
	***************************************

FIGURE 6 (Cont'd)

118	ANSMLSTIQKTFVTSSVTNHHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY ANSMLSTIQKTFVTSSVTNHHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY ANSMLSTIQKTFVTSSVTNHHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY ***********************************
83 89 108 118	NYAKAVNQKVQQLSYGGGIDLLLDFITTYSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS NYAKAVNQKVQQLSYGGGIDLLLDFITTYSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS NYAKAVNQKVQQLSYGGGIDLLLDFITTYSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS ************************************
83 89 108 118	YYVLNKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVVSSGGDYTNSFVFNEGA YYVLNKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVVSSGGDYTNSFVFNEGA YYVLNKVKGSGNLDVATGLNYRXKHSKYSVGISIPLIQRKASVVSSGGDYTNSFVFNEGA
83 108 118	SHFKVFFNYGGCF SHFKVFFNYGWVF SHFKVFFNYGWVF

8/9

aaSeqID 80	WI KEOKI DI LEVETI VNOCENTA DELOCK A
112	VLKFQKLPLLFVSILYNQSPLLAFDYKFSGVAESVSKVGFNHSKLNSKEGIFPTATFVTA
112	VSYDNTDDYYFPRIGVIFSSYATMSGLPSSGTLNSW
	· * · · * · · · · · · · · · · · · · · ·
	BLOCK B
80	TIKLQVDSNLLPKNIEKHSLKIGVGGILGALAYDSTKTLIDQATHQIYGSELFYLIGRWW
112	NGGGNVRNTKVYGKFAYHHLQKYLLIDLIARFK
	# ##
80	CEI CNA DUIVAGI TAGAN MARANA
112	GFLGNAPWKDSLIESDAHTRNYVLYNSYLFYSYGDKFHLKLGRYLSNMDFMSSYTQGFEL
112	TQGGYIFRYNTDDYLPLNSTFYMGGVTTVRGFRNG
	* * * * * * * * * * * * * * * * * * * *
	BLOCK C
80	DYKINSKIALKWFSSFGRALAFGQWIRDWYAPIVTEDGRKEVYDGIHAAQLYFSSKHVQV
112	GDGIFTASTELS
	* ** * *
	·
80	MPFAYFSPKIYGAPGVKIHIDSNPKFKGLGLRAQTTINVIFPVYAKDLYDVYWRNSKIGE
112	YGWINDAMINE NURRENDERS WINDERS OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF THE STATE OF
	YGVLKAAKMRLAWFFDFGFLTFKTPTRGSFFYN
	BLOCK D
80	
112	WGASLLIHQREDYNEFNFGFGYYQNFGNANARIGWYGNPIPFNYRNNSVYGGVFSNAITA
112	APTTTANFKDYGVVGAGFERATWRASTGLQIEWISPMGPLVL
	· · · · · · · · · · · · · · · · · · ·
80	DAVSGYVFGGGVYRGFLWGILGRYTYATRASERSINLNLGYKWGSFARVDVNLEYYVVSM
112	OWGD
•	* *
	BLOCK E
80	HNGYRLDYLTGPFNKAFKADAQDRSNLMVSMKFFF
112	GNGKKCKGLCFNPNMNDYTQHFEFSMGTRF
	** * ** *

FIGURE 7

aa SeqID# 81 MGCSFIFKKVRVYSKMLVALGLSSVLIGCAMNPSAETKKPNDAKNQQPVQTHERMTTSSE 130 MKTNGHFKDF-AWKKCFLGASVVALLVGCSPHIIETNEVALKLNYHPASE *	BLOCK A  HVTPLDFNYPVHIVQAPQNHHVVGILMPRIQVSDN-LKPYIDKFQDALINQIQTIFEKRG  KVQALDEKILLLRPAFQYSDNIAKEYENKFKNQTTLKVEEILQNQG  * **	BLOCK B YQVLRFQDEKALNVQDKKKIFSVLDLKGWVGILEDLKMNLKDPNSPNLDTLVDQSS  YKVINVDSSDKDDFSFAGKKEGYLAVAMNGEIVLRPDPKRTIQKKSEP5LLFSTGLDKME  * * * * * * * * * * * * * * * * * * *	BLOCK C GSVWFNFYEPESNRVVHDFAVEV GTFQAITYTYTSTNNASGGFNSSKSVIHENL  RVLIPAGFVKVTILEPMSGESLDSFTMDL SELDIQEKFLKTTHSSHSGGLVSTMVKGT  * * * * * * * * * * * * * * * * * * *	DKNREDAIHKILNRMYAVVMKKAVTHLTKENIAKYRDAIDRMKGFKSSMPOKK D-NSNDAIKSALNKIFASIMQEMDKHLTQRNLESYQKDAKELKNKRNR  * * * * * * * * * * * * * * * * *
aa 8 81 130	81 130	81	81	81 130

FIGURE 8

## INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

A. CLASSIFICATION OF SUBJECT MATTER  IPC(6) :A01N 43/04; A61K 31/70; C12Q 1/68				
US CL :514/44; 435/6	Patent Classification (IPC) or to both	h national classification and IPC		
	<del> </del>			
	<del></del>	-d by classification symbols		
	earched (classification system follow	ed by classification symbols;	•• •	
U.S. : 514/44; 435/6			• • •	
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched GENEBANK				
Electronic data base consu NONE	lted during the international search (r	name of data base and, where practicable	e, search terms used)	
c. DOCUMENTS CO	NSIDERED TO BE RELEVANT			
Category* Citation of	of document, with indication, where a	appropriate, of the relevant passages	Relevant to claim No.	
and Demo	onstration of Diversity at the	licobacter pylori Genome Map ne Genome Level. Journal of 74, No. 21, pages 6800-6806,	1-65	
Helicobac Nucleic A	ter pylori detected by PCR	y among clinical isolates of the based RAPD fingerprinting. 20, No. 19, pages 5137-5142,	1-65	
		5		
			٠.	
		·		
Further documents	are listed in the continuation of Box	C. See patent family annex.		
"A" document defining the				
to be of particular rele  *E" earlier document publ	syance ished on or after the international filing date	"X" document of particular relevance, the	claimed invention cannot be	
*L* document which may	throw doubts on priority claim(s) or which is publication date of another citation or other	considered novel or cannot be considered to involve an inventive step which is when the document is taken alone or other		
• • • • •	special reason (as specified)  "Y"  document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document of combined with one or more other such documents, such combination		step when the document is documents, such combination	
	ior to the international filing date but later than	*&* document member of the same patent		
	on of the international search	Date of mailing of the international sea	rch report	
27 FEBRUARY 1998	27 FEBRUARY 1998 1 3 MAR 1998			
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231  Authorized officer GINNY PORTNER				
csimile No. (703) 305-3230 Telephone No. (703) 308-0196				

# INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

Box 1 Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. X As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:  1-65, SEQ. ID Nos. 1, 7, 8, 11, 37, 39, 43, 45, 55, 61, 74, 80, 81 and 112
No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
X No protest accompanied the payment of additional search fees.

### INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-26, 47, 49, 51, 53, 55, 57, 59, and 61, drawn to no fewer than 135 nucleic acid molecules, vectors containing the nucleic acid molecules, DNA encoding fragments of the polypeptides encoded by the no fewer than 135 different DNAs, organism transformed with the nucleic acid molecules, vaccines and methods of producing polypeptides encoded by the no fewer than 135 different nucleic acid molecules.

Group II, claim(s) 27-46, 48, 50, 52, 54, 56, 58, 60, and 62-65 are, drawn to no fewer than 73 polypeptides encoded by a subset of the encoding DNA mentioned in Group I.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

Group I contains a separate DNA species for each sequence mentioned. Therefore, there is a minimum of 135 species.

Group II contains at least one polypeptide for each DNA sequence mentioned. Therefore, this is a minimum of 73 species in Group II.

For either Group that applicant elects, a total of 10 (ten) specified sequences will be searched and no more than 4 (four) specified sequences will be searched for each additional fee paid; if no additional fee is paid and no election indicated the first 10 sequences appearing in Group I will be searched.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The polypeptide encoding DNAs, vectors containing them, organisms transformed with them and methods of polypeptide production using them of Group I are materially different from each other and are therefore independent from the polypeptides of Group II. Additionally, none of the products or methods of Group I is needed to make the polypeptides of Group II.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: There is no relationship between or among the various nucleotide and amino acid sequences mentioned in the claims.

THIS PAGE BLANK (USPTO)